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**UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION**  
Washington, DC 20549  
**Form 10-K**

(Mark One)

ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the fiscal year ended December 31, 2023

TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the transition period from \_\_\_\_\_ to \_\_\_\_\_

COMMISSION FILE NO. 001-36714

**JAGUAR HEALTH, INC.**

(Exact name of registrant as specified in its charter)

Delaware  
(State or other jurisdiction of  
incorporation or organization)

46-2956775  
(I.R.S. Employer  
Identification No.)

200 Pine Street, Suite 400  
San Francisco, California 94104  
(Address of principal executive offices)

Registrant's telephone number, including area code:  
( 415 ) 371-8300

SECURITIES REGISTERED PURSUANT TO SECTION 12(b) OF THE ACT:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, Par Value \$0.0001 Per Share	JAGX	The Nasdaq Capital Market

SECURITIES REGISTERED PURSUANT TO SECTION 12(g) OF THE ACT: None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes  No

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. Yes  No

Indicate by check mark whether the registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes  No

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes  No

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K.

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer

Accelerated filer

Non-accelerated filer

Smaller reporting company

Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report.

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements.

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to §240.10D-1(b).

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes  No

As of June 30, 2023, the aggregate market value of the registrant's common stock held by non-affiliates was approximately \$ 9.9 million based upon the closing sales price of the registrant's common stock on The Nasdaq Capital Market on such date.

The number of shares of the registrant's common stock outstanding as of April 1, 2024, was 276,216,260 shares of voting common stock and 9 shares of non-voting common stock, par value \$0.0001 per share (convertible into 9 shares voting common stock)

**DOCUMENTS INCORPORATED BY REFERENCE**

Portions of the proxy statement for the registrant's 2023 Annual Meeting of Stockholders, or Proxy Statement, to be filed within 120 days of the end of the fiscal year ended December 31, 2023 are incorporated by reference in Part III hereof. Except with respect to information specifically incorporated by reference in this Form 10-K, the Proxy Statement is not deemed to be filed as a part hereof.

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TABLE OF CONTENTS

Item No.	Page No.
<b>PART I</b>	
<a href="#">Item 1. Business</a>	1
<a href="#">Item 1A. Risk Factors</a>	34
<a href="#">Item 1B. Unresolved Staff Comments</a>	68
<a href="#">Item 1C. Cybersecurity</a>	68
<a href="#">Item 2. Properties</a>	69
<a href="#">Item 3. Legal Proceedings</a>	69
<a href="#">Item 4. Mine Safety Disclosure</a>	69
<b>PART II</b>	
<a href="#">Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities</a>	70
<a href="#">Item 6. Selected Financial Data</a>	70
<a href="#">Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations</a>	70
<a href="#">Item 7A. Qualitative and Quantitative Disclosures About Market Risk</a>	82
<a href="#">Item 8. Financial Statements and Supplementary Data</a>	83
<a href="#">Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure</a>	142
<a href="#">Item 9A. Controls and Procedures</a>	142
<a href="#">Item 9B. Other Information</a>	143
<b>PART III</b>	
<a href="#">Item 10. Directors, Executive Officers and Corporate Governance</a>	143
<a href="#">Item 11. Executive Compensation</a>	143
<a href="#">Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters</a>	143
<a href="#">Item 13. Certain Relationships and Related Transactions, and Director Independence</a>	143
<a href="#">Item 14. Principal Accountant Fees and Services</a>	143
<b>PART IV</b>	
<a href="#">Item 15. Exhibits, Financial Statement Schedules</a>	144
<a href="#">SIGNATURES</a>	153

## PART I

### Forward-looking statements

This Form 10-K contains forward-looking statements within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. All statements other than statements of historical facts contained in this Form 10-K, including statements regarding our future results of operations and financial position, business strategy, prospective products, product approvals, research and development costs, timing of receipt of clinical trial, field study and other study data, and likelihood of success, commercialization plans and timing, other plans and objectives of management for future operations, and future results of current and anticipated products are forward-looking statements. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements.

In some cases, you can identify forward-looking statements by terms such as "may," "will," "should," "expect," "plan," "aim," "anticipate," "could," "intend," "target," "project," "contemplate," "believe," "estimate," "predict," "potential" or "continue" or the negative of these terms or other similar expressions. The forward-looking statements in this Form 10-K are only predictions. We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our business, financial condition and results of operations. These forward-looking statements speak only as of the date of this Form 10-K and are subject to a number of risks, uncertainties and assumptions described under the sections in this Form 10-K titled "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" and elsewhere in this Form 10-K. Forward-looking statements are subject to inherent risks and uncertainties, some of which cannot be predicted or quantified and some of which are beyond our control. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Moreover, we operate in a dynamic industry and economy. New risk factors and uncertainties may emerge from time to time, and it is not possible for management to predict all risk factors and uncertainties that we may face. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.

Jaguar Health, our logo, Napo Pharmaceuticals, Napo Therapeutics, Mytesi, Equilevia, Canalevia, Canalevia-CA1, Canalevia-CA2, and Neonorm are our trademarks that are used in this Form 10-K. This Form 10-K also includes trademarks, tradenames and service marks that are the property of other organizations. Solely for convenience, trademarks and tradenames referred to in this Form 10-K appear without the ©, ® or ™ symbols, but those references are not intended to indicate that we will not assert, to the fullest extent under applicable law, our rights or that the applicable owner will not assert its rights, to these trademarks and tradenames.

### ITEM 1. BUSINESS

#### BUSINESS

Jaguar Health, Inc. ("Jaguar") is a commercial-stage pharmaceuticals company focused on developing novel proprietary prescription medicines sustainably derived from plants from rainforest areas for people and animals with gastrointestinal ("GI") distress. Jaguar family company Napo Pharmaceuticals, Inc. ("Napo") focuses on developing and commercializing human prescription pharmaceuticals for essential supportive care and managing neglected gastrointestinal symptoms across multiple complicated disease states. Napo's crofelemer drug product candidate is the subject of the OnTarget study, a pivotal Phase 3 clinical trial for prophylaxis (prevention) of diarrhea in adult cancer patients receiving targeted therapy with or without standard chemotherapy, an indication we also refer to as preventive treatment of chemotherapy-induced overactive bowel ("CIOB")—which includes symptoms such as chronic and/or episodic debilitating diarrhea (loose and/or watery stools), urgency, bowel incontinence and abdominal pain and discomfort. Jaguar family company Napo Therapeutics, S.p.A is an Italian corporation Jaguar established in Milan, Italy in 2021 focused on expanding crofelemer access in Europe, specifically for orphan and/or rare diseases. Jaguar

Animal Health is a Jaguar tradename. Magdalena Biosciences, a joint venture formed by Jaguar and Filament Health Corp. with funding from One Small Plant Capital LLC that emerged from Jaguar's Entheogen Therapeutics Initiative ("ETI"), is focused on developing novel prescription medicines derived from plants for mental health indications.

Jaguar was founded in San Francisco, California, as a Delaware corporation on June 6, 2013 ("inception"). The Company was a majority-owned subsidiary of Napo until the close of the Company's initial public offering on May 18, 2015. The Company was formed to develop and commercialize first-in-class prescription and non-prescription products for companion animals.

On July 31, 2017, Jaguar completed a merger with Napo pursuant to the Agreement and Plan of Merger dated March 31, 2017, by and among Jaguar, Napo, Napo Acquisition Corporation ("Merger Sub"), and Napo's representative (the "Merger Agreement"). In accordance with the terms of the Merger Agreement, upon the completion of the merger, Merger Sub merged with and into Napo, with Napo surviving as the wholly owned subsidiary (the "Merger" or "Napo Merger"). Immediately following the Merger, Jaguar changed its name from "Jaguar Animal Health, Inc." to "Jaguar Health, Inc." Napo now operates as a wholly owned subsidiary of Jaguar focused on human health, including the ongoing development of crofelemer and commercialization of Mytesi.

Crofelemer is a novel, first-in-class anti-secretory antidiarrheal drug that has a normalizing effect on electrolyte and fluid balance in the gut, and this mechanism of action has the potential to benefit multiple disorders that cause gastrointestinal distress, including diarrhea and abdominal discomfort. Crofelemer is in development for multiple possible follow-on indications, including for our lead Phase 3 program in cancer therapy-related diarrhea ("CTD"), investigating prophylaxis of diarrhea related to targeted therapy with or without standard chemotherapy. Crofelemer delayed-release tablets are also being evaluated in diarrhea-predominant irritable bowel syndrome ("IBS-D") and being evaluated for chronic idiopathic/functional diarrhea. Crofelemer powder for oral solution is being developed to support orphan or rare disease indications for adults with SBS with intestinal failure and for pediatric microvillus inclusion disease ("MVID") patients. In addition, a second-generation proprietary anti-secretory antidiarrheal drug ("NP-300") is in development for symptomatic relief and treatment of moderate-to-severe diarrhea, with or without concomitant antimicrobial therapy, from bacterial, viral, and parasitic infections, including *Vibrio cholerae*, the bacterium that causes cholera. This program is being pursued with the potential targeted incentive from the US Food and Drug Administration ("FDA") for a tropical disease priority review voucher.

Napo's marketed drug Mytesi, crofelemer 125 mg delayed-release tablets, is a first-in-class oral botanical drug product approved by the FDA for the symptomatic relief of noninfectious diarrhea in adults with HIV/AIDS on antiretroviral therapy. To date, this is the only oral plant-based botanical prescription medicine approved under the FDA's Botanical Guidance. The Company's Canalevia-CA, crofelemer delayed-release tablets drug, is the first and only oral plant-based prescription product that is FDA conditionally approved to treat chemotherapy-induced diarrhea ("CID") in dogs.

In October 2020, Napo initiated its pivotal OnTarget Phase 3 clinical trial of crofelemer. The global OnTarget clinical trial is a 24-week (two 12-week stages), randomized, placebo-controlled, double-blind study to evaluate the safety and efficacy of crofelemer in diarrhea prophylaxis in adult solid tumor patients receiving targeted therapies with or without standard chemotherapy. Such prophylaxis would potentially impact the patient's ability to remain on their cancer therapy regimens at approved doses for better cancer treatment outcomes, with less required medical intervention and cost.

Patients were randomized to receive either crofelemer or matching placebo treatment that started concurrently with the initiation of a targeted cancer therapy regimen. The assessment of prophylactic effects on diarrhea will be measured by the average number of weekly loose and/or watery stools for the active crofelemer or placebo arms over the 12-week Stage I treatment period.

A significant proportion of patients undergoing cancer therapy experience diarrhea, which has the potential to cause dehydration, potential hospitalization, and non-adherence to treatment in this population. Novel "targeted cancer therapy" agents, such as epidermal growth factor receptor ("EGFR") antibodies and tyrosine kinase inhibitors ("TKIs"), with or without cycle chemotherapy agents, may cause increased electrolyte and fluid content in the gut

lumen, which results in passage of loose/watery stools (i.e., diarrhea). Diarrhea has been reported as one of the most common side effects of TKIs and may result in cancer therapy drug holidays or reductions from therapeutic doses, potentially impacting patient outcomes. Diarrhea is also a common side effect of some approved CDK 4/6 inhibitors.

With increased approval of several novel targeted therapies, it is estimated that 13.6% of cancer patients in 2020 were eligible for targeted therapies with or without standard chemotherapy regimens, according to a paper published in April 2021 in the journal *Annals of Oncology*. According to the National Cancer Institute, in 2020, 1,806,590 new cancer cases were diagnosed, and nearly 250,000 of these newly diagnosed patients could be eligible for available targeted therapies.

Due to the chronic dosing and toxicity associated with targeted therapies, many cancer patients on targeted therapy require drug holidays or dose reductions in their therapy, including those due to diarrhea. By improving stool consistency and reducing the frequency of loose/watery stools, crofelemer is expected to provide improved adherence to the therapeutic dosing of any targeted therapies, potentially leading to better clinical outcomes. We have learned from discussions with cancer drug manufacturers that the adoption and continued use of targeted cancer therapies is directly related to the ability of patients to tolerate these therapies—highlighting the importance of supportive care drugs like crofelemer to help manage cancer treatment-related diarrhea in this patient population.

As previously announced, it has been reported that patients with cancer-related diarrhea (“CRD”) were 40% more likely to discontinue chemotherapy or targeted therapy than patients without CRD. The persistence of index cancer therapy and the time to switch were also lower for patients with CRD. Strategies to control CRD and continue cancer therapy are urgently needed.

Furthermore, it has been reported that patients with CRD used significantly more resources, including outpatient services, emergency room visits, and hospitalizations. Effective prevention of CRD provides an untapped market opportunity to reduce the overall cost of cancer care. Findings from studies have indicated that patients with CRD had nearly 2.9 times higher all-cause total cost of care than patients without CRD after adjusting for covariates. Thus, prophylaxis of CRD is expected to result in a significant reduction in cancer treatment costs.

As previously announced, results from a dog study of crofelemer and an irreversible pan-HER2+TKI, neratinib, provide further scientific support for the evaluation of crofelemer in providing symptomatic relief of watery diarrhea in patients receiving a targeted cancer therapy drug like neratinib with or without cycle chemotherapy, without the use of loperamide, an antimotility drug.

The dog study was conducted without the prophylaxis or concomitant use of loperamide and demonstrated that crofelemer caused an approximate 30% reduction in the incidence and severity of diarrhea associated with daily oral administration of neratinib within the 28-day treatment period. Crofelemer also demonstrated significant improvement in the proportion of “responder” dogs, and there was a trend for fewer neratinib dose reductions in crofelemer treatment groups compared to the control group.

Crofelemer was evaluated in Phase 2 clinical study called HALT-D, for the effectiveness of crofelemer for the reduction of diarrhea in HER2-positive breast cancer patients receiving trastuzumab, pertuzumab, and chemotherapy agents such as docetaxel or paclitaxel with or without carboplatin. These therapies cause diarrhea in up to 80% of breast cancer patients, reaching grade 3, which often requires hospitalization, in 8-12% of patients. No antidiarrheal medications that specifically target the underlying mechanism of CID associated with pertuzumab-containing regimens are currently approved. The results of the study were published in October 2022 and showed that prophylaxis with crofelemer resulted in a substantial reduction of higher-grade diarrhea compared to the standard-of-care control group patients.

Recent studies have shown that EGFR inhibitors cause increased chloride secretion into the lumen of the gut and that crofelemer, through its unique and novel mechanism of normalizing the chloride-secretory actions of the cystic fibrosis transmembrane conductance regulator (“CFTR”) and calcium-activated chloride channels (“CaCC”), is

considered to be mechanistically- and physiologically-appropriate for reducing the loss of electrolyte and fluid in breast cancer patients receiving this regimen.

As announced on October 26, 2022, the results of the HALT-D trial were published in the peer-reviewed journal *Breast Cancer Research and Treatment*.

This HALT-D study evaluated 51 breast cancer patients eligible to receive at least three cycles of pertuzumab-containing regimen with chemotherapy that were randomly assigned to either crofelemer in cycles 1 and 2 or the control group, in which patients received standard of care. Breakthrough anti-diarrheal medicines ("BAM") were permitted but not given prophylactically. Findings showed that the primary endpoint, the incidence of diarrhea for at least two consecutive days, was not statistically different for the two groups. However, crofelemer patients demonstrated significantly better outcomes compared to control group patients across a number of key secondary endpoints, including reductions in the incidence and severity of diarrhea in cycle two based on Investigator and Patient Reported Outcomes (see Jaguar Health's November 19, 2021 press release). The study also showed that CID occurred significantly less (by 23%) in the crofelemer group during cycle 1, and crofelemer patients were 1.8 times more likely than control patients to have their diarrhea resolved. These data provide proof-of-concept ("POC") support to the primary endpoint in Napo's phase 3 OnTarget clinical study.

Crofelemer was granted Orphan Drug Designation ("ODD") by the FDA in February 2023 for MVID—an ultra-rare congenital diarrheal disorder ("CDD")—and granted ODD for MVID by the European Medicines Agency ("EMA") in October 2022. Crofelemer was granted ODD for short bowel syndrome ("SBS") by the EMA in December 2021 and by the FDA in August 2017. In August 2023, the FDA activated Napo's Investigational New Drug ("IND") application for a new crofelemer powder for oral solution formulation for the treatment of MVID. In 2024, Jaguar Jaguar expects to initiate pediatric MVID clinical studies, on three continents for the rare disease indications of MVID, CDD, SBS. In accordance with the guidelines of specific European Union countries, published data from such clinical investigations could support reimbursed early patient access to crofelemer for these debilitating conditions in 2025 while the company pursues approval of crofelemer for SBS and MVID from the EMA and the FDA. Participation in early access programs, which do not exist in the US, provides an opportunity for reimbursement while impacting the morbidity and high cost of care for these chronic unmet needs.

The Orphan Drug Act ("ODA") in the US grants special status to a small molecule drug or biological product to treat a rare disease or condition upon request of a sponsor. This status is referred to as ODD (or sometimes "orphan status"). ODD qualifies the drug's sponsor for various development incentives, including tax credits for qualified clinical testing and relief of filing fees. Additionally, the ODA provides a seven-year period of marketing exclusivity to the first sponsor who obtains marketing approval for a designated orphan drug.

In the EU, receipt of ODD supports some specific regulatory pathways, and sponsors who obtain ODD for their drug can benefit from Scientific Advice from the EMA for clinical trials for the orphan indication and receive market exclusivity for a period of ten years once the medicine is approved for commercialization.

CDDs are a group of rare, chronic intestinal channel diseases, with onset in early infancy, that are characterized by severe, lifelong diarrhea and a lifelong need for nutritional intake either parenterally or with a feeding tube. CDDs are related to specific genetic defects inherited as autosomal recessive traits. The incidence of CDDs is prevalent in regions where consanguineous marriage (related by blood) is part of the culture. CDDs are directly associated with serious secondary conditions, including dehydration, metabolic acidosis, and failure to thrive, prompting the need for immediate therapy to prevent death and limit lifelong disability.

SBS affects approximately 10,000 to 20,000 people in the US, according to the Crohn's & Colitis Foundation, and it is estimated that the population of SBS patients in Europe is approximately the same size. Despite limited treatment options, the global SBS market exceeded \$568 million in 2019 and is expected to reach \$4.6 billion by 2027, according to a report by Vision Research Reports.

MVID is considered an ultra-rare CDD, with likely a couple of hundred patients diagnosed globally. In February 2022, Napo announced the completion of an investigator-initiated preclinical enterocyte (intestinal cell) *in vitro* study to evaluate the effects of crofelemer on cells with certain genetic defects that result in specific forms of MVID. MVID patients have intestinal failure and morbidity resulting in a failure to thrive due to malabsorption of nutrients and need parenteral nutrition. We believe the novel mechanism of action of crofelemer may have considerable potential to manage the severe secretory loss of electrolytes and fluid resulting in dehydration. There are currently no therapies for MVID except parenteral nutrition. Thus, crofelemer may reduce the associated morbidity and mortality of MVID and lessen the need for parenteral nutrition ("PN").

Most of the activities of the Company are focused on the development and/or commercialization of Mytesi, the ongoing clinical development of crofelemer for the prophylaxis of diarrhea in adult patients receiving targeted cancer therapy, and our prioritized clinical program centered around investigator-initiated POC trials of SBS and MVID.

In January 2023, Jaguar and Filament Health, with funding from One Small Planet, formed the US-based joint venture Magdalena Biosciences ("Magdalena"). Magdalena's focus is on the development of novel, natural prescription medicines derived from plants for mental health indications, including, initially, attention-deficit/hyperactivity disorder ("ADHD") in adults. The goal of the collaboration is to extend the botanical drug development capabilities of Jaguar and Filament in order to develop pharmaceutical-grade, standardized drug candidates for mental health disorders and to partner with a potential future licensee to develop and commercialize these novel plant-based drugs. This venture aligns with Jaguar's ETI program and Filament's corporate mission to develop novel, natural prescription medicines from plants. Magdalena is leveraging Jaguar's proprietary medicinal plant library and Filament's proprietary drug development technology. Jaguar's library of 2,300 highly characterized medicinal plants and 3,500 plant extracts, all from firsthand ethnobotanical investigation by Jaguar and members of the ETI Scientific Strategy Team, is a key asset our team has generated over 30 years that bridges the knowledge of traditional healers and Western medicine. Magdalena holds an exclusive license to plants and plant extracts in Jaguar's library, not including any sources of crofelemer or NP-300, for specific indications and is in the process of identifying plant candidates in the library that may prove beneficial for addressing indications such as ADHD.

The Company also launched the ETI initiative to support the discovery and development of novel, natural medicines derived from psychoactive and psychedelic plant compounds for the treatment of mood disorders, neurodegenerative diseases, addiction, and other mental health disorders. The initiative is initially focused on plants with the potential to treat depression and leverages Napo's proprietary library of approximately 2,300 plants with medicinal properties. According to statistics available from the National Institute of Mental Health Disorders, part of the National Institutes of Health, approximately 9.5% of American adults ages 18 and over will suffer from a depressive illness (major depression, bipolar disorder, or dysthymia) each year.

Field research collaborations have been conducted in the past by members of the scientific strategy team ("SST") of Jaguar's predecessor company Shaman Pharmaceuticals, who are also members of the ETI SST, and have yielded possible applications for a compound called alstonine. Alstonine is derived from a plant used by traditional healers in Nigeria and has demonstrated a potential novel mechanism of action for the treatment of difficult-to-manage conditions such as schizophrenia.

The ETI SST consists of leading and globally renowned ethnobotanists, physicians, pharmacologists, and experts in natural product chemistry and neuropharmacology. We believe the wealth of expertise, experience, and commitment of the ETI SST—comprised of multiple members of the original SST that contributed to the development of Jaguar's proprietary library of plants—will play an instrumental role in advancing our shared initial goal of identifying plants in our library that may have the potential to treat mood disorders and neurodegenerative diseases, such as Alzheimer's disease, Parkinson's disease, and amyotrophic sclerosis. Mood disorders and neurodegenerative diseases affect hundreds of millions of people around the globe and represent classic unmet medical needs.

In the field of animal health, we are continuing limited activities related to developing and commercializing first-in-class gastrointestinal products for dogs, dairy calves, and foals. In December 2021, we received conditional approval from the FDA to market Canalevia-CA1 (crofelemer delayed-release tablets), our oral plant-based

prescription drug and the only available veterinary drug for the treatment of CID in dogs, and Canalevia-CA1 is now available to multiple leading veterinary distributors in the US, including Chewy. Canalevia-CA1 is a tablet given orally and can be prescribed for home treatment of CID. The FDA conditionally approves Canalevia-CA1 under application number 141-552. Conditional approval allows for product commercialization while Jaguar Animal Health continues to collect the substantial evidence of effectiveness required for full approval. We have received a Minor Use in a Major Species ("MUMS") designation from the FDA for Canalevia-CA1 to treat CID in dogs. FDA has established a "small number" threshold for minor use in each of the seven major species covered by the MUMS Act. The small number threshold is currently 80,000 for dogs, representing the largest number of dogs that can be affected by a disease or condition over the course of a year and still have the use qualify as a minor use.

Napo completed its requisite preclinical and formulation activities to support the IND application for its second-generation, plant-based oral prescription drug product, NP-300, for its clinical development for the symptomatic relief and treatment of moderate-to-severe diarrhea, with or without concomitant antimicrobial therapy, from bacterial, viral and parasitic infections including *Vibrio cholerae*, the bacterium that causes cholera. As announced in September 2022, the FDA has activated the Company's IND application for NP-300, and the FDA concluded that Napo may proceed with its proposed phase 1 clinical trial for NP-300. Following the completion of the phase 1 trial, the Company will be positioned to initiate the next stage of our clinical development program for cholera-related diarrhea when our development team has the requisite resources and bandwidth to initiate the additional required trials.

Cholera produces a devastating loss of electrolytes and fluid in patients, and without appropriate reduction in loss of fluid and electrolytes, patients experience significant hospitalization and mortality. NP-300 provides the opportunity to treat cholera patients in combination with oral rehydration salts ("ORS") and the recommended guidelines from the World Health Organization ("WHO") for the use of appropriate antibiotics to reduce the burden of the pathogen. Appropriate preclinical toxicity studies and formulation development activities are ongoing to support the conduct of clinical studies with NP-300.

Napo received partial financial support for preclinical services from the National Institute of Allergy and Infectious Diseases ("NIAID") of the National Institutes of Health, and Napo is grateful for their support of NP-300's development.

Cholera is an acute diarrheal illness caused by intestine infection with the bacterium *Vibrio cholerae*. According to the Centers for Disease Control and Prevention of the US Department of Health & Human Services, an estimated 1.3 to 4 million people around the world get cholera each year, and 21,000 to 143,000 people die from it. The infection is often mild or without symptoms but can sometimes be severe. Approximately one in ten infected persons will have severe disease characterized by profuse, watery diarrhea, vomiting, and leg cramps. In these people, rapid loss of body fluids leads to dehydration and shock. Without treatment, death can occur within hours. Cholera is now endemic in many countries outside the US. Preliminary data issued January 11, 2024, by WHO indicates that the number of cholera cases reported in 2023 in WHO Member States as of December 15, 2023, surpassed that of 2022. Nearly a year has passed since WHO classified the global resurgence of cholera as a grade 3 emergency, the highest internal level for a health emergency requiring a comprehensive response at the three levels of the organization.

We expect that NP-300 will be significantly less expensive and would support development efforts to receive a tropical disease priority review voucher from the FDA for an indication of the symptomatic treatment of diarrhea from acute infections such as cholera. The FDA grants priority review vouchers as an incentive to develop treatments for neglected diseases and rare pediatric diseases. Priority review vouchers are transferable and, in past transactions by other companies, have sold for prices ranging from \$60 million to \$350 million. Additionally, we believe NP-300 may provide a long-term pipeline opportunity as a second-generation anti-secretory agent for multiple gastrointestinal diseases—especially in resource-constrained countries.

The NP-300 program is paired with funding from a promissory note related to the potential future sale of a possible tropical disease priority review voucher ("TDPRV").

Napo has actively ensured that its intellectual property ("IP") filings in support of the development of crofelemer for various proposed indications are protected appropriately. The IP portfolio for crofelemer includes the relief and treatment of HIV-associated diarrhea and CID as well as planned indications for inflammatory diarrhea, IBS-D, CDD, and SBS, with all indications, Napo prioritizes IP protection. Napo currently holds approximately 148 patents, the majority of which do not expire until 2027-2031, and approximately 50 patents pending.

While Napo and Jaguar remain steadfastly focused on the commercial success of Mytesi and on the potential development of crofelemer for CTD and the rare disease indications of SBS with intestinal failure and CDD, the Company believes the same competencies and multi-disciplinary scientific strategy that led to the successful development of Mytesi will support collaborative efforts with potential partners—such as the recently formed joint venture Magdalena Biosciences—to develop novel first-in-class prescription medicines derived from plants.

Our management team has significant experience in gastrointestinal product development for both humans and animals. Napo was founded more than 30 years ago to perform drug discovery and development by leveraging the knowledge of traditional healers working in rainforest areas. Ten Jaguar and Napo team members have been together for more than 15 years. Dr. Steven King, our chief sustainable supply, ethnobotanical researcher, and intellectual property officer, and Lisa Conte, our founder, president, and CEO, have worked together for over 30 years. We have buttressed the early founding team with the expertise and experiences of team members like Dr. Darlene Horton and Dr. Karen Brunke to support the Napo and Jaguar family's continued development and commercialization activities. We have assembled an impressive group of scientific advisory board ("SAB") members who work closely with the Chair of Jaguar's Scientific Advisory Board, Dr. Pravin Chaturvedi, who also serves as the Chief Scientific Officer ("CSO") of Jaguar. Together, these dedicated personnel successfully transformed crofelemer, extracted from trees growing in the rainforest, to Mytesi and Canalevia-CA1, natural, sustainably harvested, FDA-approved drugs.

We believe Jaguar is poised to realize a number of synergistic, value-adding benefits—an expanded pipeline of potential blockbuster human follow-on indications of crofelemer, and a second-generation anti-secretory agent—upon which to build global partnerships. Jaguar, through Napo, holds global unencumbered rights for crofelemer, Mytesi, and Canalevia-CA1. Additionally, several drug product opportunities in Jaguar's crofelemer pipeline are backed by Phase 2 and POC evidence from human clinical trials.

#### **Pipeline development opportunities for crofelemer**

Crofelemer is currently being evaluated for the prophylaxis of CTD in adult solid tumor patients receiving targeted therapy with or without standard chemotherapy. A significant proportion of patients undergoing cancer therapy experience diarrhea. Novel targeted cancer therapy agents, such as epidermal growth factor receptors and tyrosine kinase inhibitors, may activate intestinal chloride secretory pathways, leading to increased chloride secretion into the gut lumen and significant water loss that would result in secretory diarrhea.

According to data appearing in "Treatment Guidelines for CID" (chemotherapy-induced diarrhea) in the April 2004 issue of *Gastroenterology and Endoscopy News*, diarrhea is the most common adverse event reported in chemotherapy patients. Approved third-party supportive care products for chemotherapy-induced nausea and vomiting ("CINV") include Sustol, Aloxi, Akyrneo, and Sancuso. According to a market research report by iHealthcareAnalyst, Inc., the global market for CINV drugs is estimated to reach a value of \$3.9 billion by 2029.

Diarrhea has been reported as the most common side effect of the recently approved CDK 4/6 inhibitor abemaciclib and the pan HER TKI neratinib, with occurrence ranging from 86% to >95% and grade 3 over 40%, in published studies. Diarrhea in this patient population has the potential to cause dehydration, potential infections, and non-adherence to treatment. In this population, a novel anti-diarrheal like crofelemer may hold promise for treating secretory diarrhea—and therefore also support long-term cancer treatment adherence.

Jaguar's and Napo's portfolio development strategy involves meeting with Key Opinion Leaders ("KOLs") to identify indications that are potentially high value because they address important medical needs that are significantly or globally unmet, obtain input on protocol practicality and protocol generation, and then strategically

sequencing indication development priorities, second-generation product pipeline development, and partnering goals on a global basis.

Mytesi is the only antidiarrheal drug that the FDA has approved for the treatment of chronic, noninfectious diarrhea in adult HIV/AIDS patients receiving antiretroviral therapy ("ART"). This approval was on the basis of the drug's safety and efficacy in reducing the number of weekly and daily watery stools in patients and improving stool consistency, from unformed to formed stools, over a 24-week treatment period.

Unlike other available diarrhea remedies, crofelemer does not act by inhibiting intestinal motility. It has minimal absorption and does not have any clinically significant food or drug interactions, thereby allowing patients to maintain their appropriate dosing of treatment to suppress their viral load and maintain adequate Cluster Differentiation 4 "CD4" levels in People Living with HIV/AIDS "PLWHA". Crofelemer is also the only approved antidiarrheal drug that is approved for chronic use. Moreover, it is not an opioid, like other traditionally used treatments, thus avoiding both the acute side effect of constipation and the potential for abuse.

There are significant barriers to entry for generic competition for Mytesi (crofelemer). Napo holds an extensive global patent portfolio. At the present time, we hold approximately 148 issued worldwide patents, with coverage in many cases that extends until 2031. These issued patents cover multiple indications, including HIV/AIDS diarrhea, irritable bowel syndrome ("IBS"), IBD, manufacturing, and enteric protection from gastric juices, among others. We also have approximately 50 pending patent applications worldwide in the human health areas that are being prosecuted.

Mytesi is the first oral drug approved under the FDA's Botanical Guidance, providing another entry barrier from potential generic competition. The FDA requires that the manufacturer of crofelemer use a validated proprietary bioassay to release the drug substance and drug product of Mytesi. While most generic products are fashioned to meet chemical release specifications that are in the public domain, the specifics of this assay are not publicly available. There is no pathway by which a generic product can be developed for a drug approved under botanical guidance. In addition, Mytesi is minimally absorbed systemically, so the classic approach of creating a generic drug by matching pharmacokinetic blood levels is not possible. A generic player would have to conduct costly and risky clinical trials.

While Jaguar's commercial and development efforts have evolved to focus primarily on Mytesi and human pipeline indications since its merger with Napo, the Company commenced launch initiatives related to Canalevia-CA1, our drug product which received conditional approval in December 2021 for treatment of CID in dogs. The same mechanism of action typically causes CID in dogs as in humans, and hence, the work in dogs serves as a preclinical POC for diarrhea in humans that is related to targeted cancer therapy. CID is an interesting model for human medical needs and is being pursued as a prescription indication for animal health. We believe there is an important unmet medical need for the treatment of CID in dogs. Certain cancer treatment agents provided to dogs are human drugs or have the same mechanism of action as human cancer drugs, and these agents and mechanisms of action often have meaningful rates of diarrhea in humans as well.

As previously announced, Jaguar has received MUMS designation status from the FDA for Canalevia-CA1 for the indication of CID in dogs. MUMS designation is modeled on the ODD for human drug development and offers possible financial incentives to encourage MUMS drug development, such as the availability of grants to help with the cost of developing the MUMS drug.

Canalevia is also the Company's drug candidate for the proposed indication of exercise-induced diarrhea ("EID") in dogs.

Crofelemer is extracted and purified from the *Croton lechleri* tree, which we sustainably harvest and manage through programs that we have been developing over the past 30 years. This process has involved working with local and indigenous communities to plant trees, obtain permits for export, and create a supply network that is robust and reliable.

Our team continues to have relationships with partners that we began working within the 1990s. Additionally, through the establishment of a nonprofit called the Healing Forest Conservancy, our team has created a long-term mechanism for benefit sharing that recognizes the intellectual contribution of Indigenous populations. This program intends to contribute to the continued strength and effectiveness of the valued and strategically important relationships we have cultivated over the past 30 years.

**Product Pipeline**

In addition to our Mytesi (crofelemer) product that the FDA approves for the symptomatic relief of noninfectious diarrhea in adults with HIV/AIDS on antiretroviral therapy, we are also developing a pipeline of prescription drug product candidates to address unmet needs in gastrointestinal health through Napo. Mytesi (crofelemer) is a novel, first-in-class anti-secretory antidiarrheal drug that has a normalizing effect of restoring the electrolyte and fluid balance in the gut and lumen, and this mechanism of action has the potential to benefit multiple disorders. Clinical trials demonstrated that nearly 80% of Mytesi users experienced an improvement in their diarrhea over a four-week period. At week 20 of the pivotal trial, over half the patients had no watery stools or a 100% decrease, and 83% had at least a 50% decrease in watery stools. Our Mytesi pipeline currently includes prescription drug product candidates for multiple follow-on indications, several of which are backed by Phase 2 evidence from clinical trials. In addition, NP-300 is in development for symptomatic relief and treatment of moderate-to-severe diarrhea, with or without concomitant antimicrobial therapy, from bacterial, viral, and parasitic infections, including *Vibrio cholerae*, the bacterium that causes cholera.

**Napo Prescription Drug Product Candidates**

<b>Product Candidates</b>	<b>Indication</b>	<b>Completed Milestones</b>	<b>Current Phase of Development</b>	<b>Anticipated Near-Term Milestones*</b>
Mytesi	CTD	<ul style="list-style-type: none"> <li>Initiated pivotal Phase 3 clinical trial in October 2020</li> </ul>	Phase 3	<ul style="list-style-type: none"> <li>Awaiting unblinding</li> </ul>
Mytesi	IBS-D	<ul style="list-style-type: none"> <li>Two Phase 2 studies completed</li> </ul>	Phase 2	<ul style="list-style-type: none"> <li>Potential business development opportunities</li> </ul>
Mytesi	Chronic idiopathic diarrhea	<ul style="list-style-type: none"> <li>Clinical POC study initiated at The University of Texas Health Science Center at Houston ("UTH")</li> </ul>	Phase 2 POC study	<ul style="list-style-type: none"> <li>Top line results expected in 2023</li> </ul>
Mytesi	Functional diarrhea	<ul style="list-style-type: none"> <li>Initiated clinical study at Beth Israel Deaconess Medical Center, Harvard Medical School, Boston</li> </ul>	Phase 2 POC study	<ul style="list-style-type: none"> <li>Enrollment ongoing</li> </ul>
Crofelemer powder for oral solution*	Rare disease indication: SBS with intestinal failure in adults	<ul style="list-style-type: none"> <li>ODD for SBS granted by FDA and EMA</li> </ul>	Clinical POC study	<ul style="list-style-type: none"> <li>IIT POC study in 2024</li> </ul>
Crofelemer powder for oral solution*	Rare disease indication: Pediatric MVID, a CDD condition	<ul style="list-style-type: none"> <li>ODD for MVID granted by FDA and EMA</li> </ul>	IND stage	<ul style="list-style-type: none"> <li>Initiating clinical study in 2024</li> </ul>
NP-300*	Second-generation antidiarrheal drug for infectious diarrhea including from <i>Vibrio cholerae</i> , the bacterium that causes cholera	<ul style="list-style-type: none"> <li>FDA activated Company's IND: Q3 2022</li> </ul>	Phase I	<ul style="list-style-type: none"> <li>Initiating Phase 1 trial</li> </ul>

\*Clinical trials are funding dependent

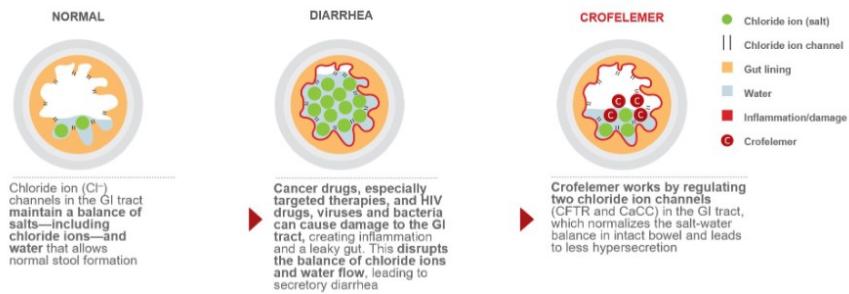
**Estimated Size of Mytesi Target Markets**

We believe the medical need for Mytesi is significant, compelling, and unmet, and that doctors are looking for a drug product with a mechanism of action that is distinct from the options currently available to resolve diarrhea. A growing percentage of HIV patients have lived with the virus in their gut for 10+ years, often causing gut enteropathy and chronic or chronic episodic diarrhea. According to data from the US Centers for Disease Control and Prevention, it was estimated that by 2020 more than 70% of Americans with HIV were 50 and older and had lived with HIV for more than 10 years (1).

Market	Competition	Market Size/Potential
HIV-related Diarrhea (Mytesi)	None	We estimate the US market revenue potential for Mytesi to be approximately \$50 million in gross annual sales.
CTD (Crofelemer delayed-release tablets)	None	An estimated 650,000 US cancer patients receive chemotherapy in an outpatient oncology clinic(2). Comparable supportive care (i.e., CINV) product sales of ~\$620 million in 2013(3). The global CINV market is projected to reach a valuation of \$2.7 billion by 2022(4).
SBS/MVID (Crofelemer powder for oral solution)	1	Financial benefits of ODD. The global SBS market exceeded \$568 million in 2019 and is expected to reach \$4.6 billion by 2027, according to a report by Vision Research Reports(5).
IBS-D (Crofelemer delayed-release tablets)	3	Most IBS products have an estimated revenue potential of greater than \$1.0 billion(6).
Infectious Diarrhea (NP-300 tablets)	None	In transactions by other companies, priority review vouchers have sold for \$67 million to \$350 million(7).

- (1) HIV Among People Aged 50 and Older (<https://www.cdc.gov/hiv/group/age/olderamericans/index.html>)
- (2) Centers for Disease Control and Prevention. Preventing Infections in Cancer Patients: Information for Health Care Providers ([cdc.gov/cancer/prevent infections/providers.htm](https://www.cdc.gov/cancer/prevent_infections/providers.htm))
- (3) Heron Therapeutics, Inc. Form 10-K for the fiscal year ended December 31, 2016
- (4) Report published by Allied Market Research, titled, "Chemotherapy-induced Nausea and Vomiting (CINV) Market-Global Opportunity Analysis and Industry Forecast, 2014-2022" (<https://www.prnewswire.com/news-releases/chemotherapy-induced-nausea-and-vomiting-cinv-market-expected-to-reach-2659-million-by-2022-611755395.html>)
- (5) Short Bowel Syndrome Market – Global Industry Analysis, Size, Share, Trends, Revenue, Forecast 2020 to 2027 (<https://www.mynewsdesk.com/us/medical-technology-news/pressreleases/short-bowel-syndrome-market-global-industry-analysis-size-share-trends-revenue-forecast-2020-to-2027-3069433>)
- (6) Merrill Lynch forecasts peak US sales of roughly \$1.5 bn for Ironwood's Linzess (<https://247wallst.com/healthcare-business/2015/04/27/key-analyst-sees-nearly-30-upside-in-ironwood/>); Rodman & Renshaw estimate peak annual sales of Synergy Pharmaceuticals' Trulance at \$2.3 bn in 2021 (<https://www.benzinga.com/analyst-ratings/analyst-color/17/04/9304883/what-synergys-new-patents-mean-for-its-commercial-prospective>)
- (7) In Aug. 2015, AbbVie Inc. bought a priority review voucher from United Therapeutics Corp for \$350 million (<https://www.wsj.com/articles/united-therapeutics-sells-priority-review-voucher-to-abbvie-for-350-million-1439981104> ). In July 2014, BioMarin announced that it had sold a priority review voucher to Sanofi and Regeneron for \$67.5 million. (<https://investors.biomarin.com/2014-07-30-BioMarin-Sells-Priority-Review-Voucher-for-67-5-Million>).

The following diagram illustrates the mechanism of action of crofelemer, which normalizes chloride ion secretion and fluid content of the gut to improve stool consistency.



### Business Strategy

Our goal is to become a leading pharmaceutical company with first in class, sustainably derived products that address significant unmet gastrointestinal medical needs globally. To accomplish this goal, we plan to:

#### ***Expand Mytesi by leveraging our significant gastrointestinal product knowledge, experience and intellectual property portfolio***

Mytesi (crofelemer 125 mg delayed-release tablets) is a novel, first-in-class anti-secretory antidiarrheal agent which has a normalizing effect on the electrolyte and fluid balance in the gut, and this mechanism of action has the potential to benefit multiple gastrointestinal disorders. Our Mytesi (crofelemer) product is approved by the FDA for the symptomatic relief of noninfectious diarrhea in adults with HIV/AIDS on antiretroviral therapy. Jaguar, through Napo and Napo Therapeutics, holds global unencumbered rights for Mytesi. Mytesi is in development for multiple possible follow-on indications, including prophylaxis of diarrhea related to targeted therapy with or without standard chemotherapy. Crofelemer delayed-release tablets are also being evaluated in IBS-D and idiopathic/functional diarrhea.

Crofelemer powder for oral solution is being developed to support orphan or rare disease indications for infants and/or children with SBS and/or CDD, such as MVID.

In addition, a NP-300 is in development for symptomatic relief and treatment of moderate-to-severe diarrhea, with or without concomitant antimicrobial therapy, from bacterial, viral and parasitic infections including *Vibrio cholerae*, the bacterium that causes cholera.

Our management team collectively has extensive experience in the development of prescription drugs. This experience covers all aspects of product development, including discovery, preclinical and clinical development, GMP manufacturing, regulatory affairs, and commercialization. Key members of this team successfully developed Mytesi.

#### ***Maintain commercial capabilities in Mytesi sales and marketing efforts***

Napo's direct sales organization is comprised of Mytesi field sales representatives strategically positioned in different territories to cover US geographies with the highest potential. With support provided by concomitant marketing, promotional activities, patient empowerment programs, including an integrated social digital campaign, and medical education initiatives described below, we expect a proportional response in the number of patients treated with Mytesi.

**Leverage our relationships with Scientific Advisory Board (SAB) members for crofelemer commercialization and development in follow-on indications**

The Company has retained several subject matter experts and KOLs as its SAB members across the therapeutic areas of HIV, CTD, gastrointestinal disorders, SBS, and/or CDD.

**Establish partnerships to support moving pipeline indications to pivotal clinical trials**

The Company's goal is to establish partnerships to support moving pipeline indications towards commercialization in the US and/or other geographies.

**Strategically sequence the development of follow-on indications of Mytesi and seek geographically focused licensing opportunities**

As announced April 1, 2022, the Company has entered an agreement with Quadri Pharmaceuticals Store LLC ("Quadri Pharma") that grants Quadri Pharma exclusive promotional, commercialization, and distribution rights for specified human indications of Mytesi (crofelemer 125 mg delayed-release tablets) in Bahrain, Kuwait, Qatar, Saudi Arabia, the United Arab Emirates ("UAE"), and Oman following regulatory approval to market crofelemer in these countries for the specified indications, including the indication currently approved in the US for HIV-related diarrhea. They also have rights to commercialization, for Mytesi for CTD, for which crofelemer is currently in a pivotal Phase 3 clinical trial. In addition, the agreement grants Quadri Pharma exclusive rights to distribute crofelemer in these countries in the immediate future under Named Patient Programs.

As announced September 24, 2018, Jaguar and Knight Therapeutics Inc. ("Knight") entered into a Distribution, License and Supply Agreement that grants Knight the exclusive right to commercialize Mytesi and related products in Canada and Israel. The License Agreement has a term of 15 years (with automatic renewals) and provides Knight with an exclusive right to commercialize current and future Jaguar human health products (including crofelemer, NP-300, and any product containing a proanthocyanidin or with an anti-secretory mechanism) in Canada and Israel. Knight forfeited its right of first negotiation for expansion to Latin America. Under the License Agreement, Knight is responsible for applying for and obtaining necessary regulatory approvals in the territory of Canada and Israel, as well as marketing, sales and distribution of the licensed products. Knight will pay a transfer price for all licensed products, and upon achievement of certain regulatory and sales milestones, the Company may receive payments from Knight in an aggregate amount of up to approximately \$1.8 million payable throughout the initial 15-year term of the agreement. The Company did not have any license revenues since the execution of this agreement.

Although it is possible that we may enter into additional corporate partnering relationships related to Mytesi, our intention would be to retain all or co-commercialization and promotional rights in the US so that we do not become primarily a royalty collecting organization, and we are opposed to entering into any Mytesi partnering relationship that would require splitting indications. We seek to put limited geographically focused partnerships in place in the near term, while also considering possibilities for a worldwide partnership with a leading global entity (excluding the US exclusive commercial rights) in the long-term field of gastrointestinal care and cancer.

**Reduce risks relating to product development**

Risk reduction is a key focus of our product development programs. Mytesi is FDA approved for a first-in-class chronic noninfectious diarrhea indication in adult HIV/AIDS patients receiving ART. This FDA approved New Drug Application ("NDA") provides us the ability to leverage this corresponding safety data when seeking approval for additional follow-on indications that are also chronic or chronic episodic indications. In an effort to reduce risk further, we have implemented the following approach: first, we meet with KOLs, including at medical conferences. Next, we confirm unmet medical needs with patients as well as KOLs and discuss the practicality of patient enrollment and trial implementation. We then generate protocols to discuss with the FDA, seeking, when possible, special protocol assessments. Our goal is to have de risked the program as much as we believe we possibly can, by the

time we start devoting significant funds to a clinical trial, in particular the regulatory pathway. We believe this approach will lead to better long-term outcomes for our products in development.

We will continue to seek partnerships outside the US for the above indications while focusing on development and commercial access in the US directly. We are also focused on investigating NP-300 for various gastrointestinal indications. NP-300 is a proprietary Jaguar pharmaceutical product, a standardized botanical extract distinct from crofelemer, also sustainably derived from the *Croton lechleri* tree.

We believe NP-300, which has a similar mechanism of action as crofelemer and is significantly less costly to produce, may support efforts to receive a priority review voucher from the FDA for symptomatic relief and treatment of moderate-to-severe diarrhea, with or without concomitant antimicrobial therapy, from bacterial, viral and parasitic infections including *Vibrio cholerae*, the bacterium that causes cholera. The FDA grants priority review vouchers to drug developers for TDPRV as an incentive to develop treatments for neglected diseases and rare pediatric diseases. Additionally, we believe NP-300 represents a long-term pipeline opportunity as a second-generation anti-secretory agent, on a global basis, for multiple gastrointestinal diseases—especially in resource constrained countries where the cost of goods is a factor, in part, because requirements often exist in such regions for drug prices to decrease annually.

The Company has previously presented Phase 2 data on crofelemer for the treatment of diarrhea in cholera patients from a study in Bangladesh. Napo plans to follow a similar clinical study design to support the development of NP-300 for a cholera-related indication. Our portfolio development strategy is based on identifying indications that are potentially high value because they address important medical needs that are significantly or globally unmet, and then strategically sequencing indication development priorities, second-generation product pipeline development, and partnering goals on a global basis.

Our technology for proprietary gastrointestinal disease products is central to the product pipelines of both human and veterinary indications. Crofelemer is also the active pharmaceutical ingredient ("API") in Canalevia-CA1, our prescription drug product conditionally approved by the FDA and launched for CID in dogs.

#### **Napo Therapeutics Provides New Opportunities to Treat Orphan Indications Like SBS**

Jaguar is strategically pursuing multiple important shots on goal for its drug development pipeline: Crofelemer for CTD, SBS, and CDDs. Jaguar's exclusive license agreement with Napo Therapeutics provides a perpetual, royalty-bearing license for Europe and includes traditional terms such as royalties on sales in Europe, and a supply agreement, and rights to utilize all data Napo Therapeutics generates for Jaguar development and approval activities globally.

#### **Competition**

Several significantly larger pharmaceutical companies are competing with us in the gastrointestinal segment.

*Diarrhea in adult patients living with HIV/AIDS.* We are not aware of any other FDA-approved drugs for the symptomatic relief of diarrhea in HIV/AIDS patients. HIV/AIDS diarrhea patients may also use loperamide or Lomotil, but these medications affect motility, which can result in rebound diarrhea and are not indicated for chronic use. Other agents' patients may use include over-the-counter anti-diarrheal remedies such as Mylanta or Kapectate.

*Cancer therapy-related diarrhea.* We are not aware of any FDA-approved drugs specifically indicated for prophylaxis of cancer therapy-related diarrhea in patients receiving targeted therapies with or without standard chemotherapy. Opioids and over-the-counter drugs are commonly used to treat chemotherapy-induced diarrhea, but these drugs affect motility. Certain tyrosine kinase inhibitor chemotherapy agents have diarrhea as a significant side effect. For example, FDA guidance suggests diarrhea prophylaxis prior to initiating adjuvant therapy with neratinib.

*CDD.* We are not aware of any FDA-approved drugs specifically indicated for CDD.

*SBS with intestinal failure.* In the US, Takeda Pharmaceuticals' GATTEX® (teduglutide) is indicated for treating adults and pediatric patients 1 year of age and older with SBS dependent on parenteral support. Zorbtive® is a recombinant human growth hormone indicated for the treatment of SBS in adult patients receiving specialized nutritional support. To the best of our knowledge, no drugs have been approved in the US or the rest of the world (ROW) to reduce parenteral support with a concomitant reduction in the high stool volume and diarrhea in SBS patients.

*Diarrhea predominant irritable bowel syndrome.* Two drugs were approved in 2015 for the treatment of diarrhea, predominantly irritable bowel syndrome, Allergan plc's Viberzi and Xifaxan, which are marketed by Valeant Pharmaceuticals International. Also, Lotronex was approved by the FDA in 2000 but was withdrawn from the market and later reintroduced in 2002 under a Risk Management Program. With the exception of Lotronex, the sponsors of Viberzi and Xifaxan employ extensive media and print promotion for the commercialization of these products.

*Infectious diarrhea.* We are not aware of any FDA-approved drugs specifically acting as anti-secretory drugs to improve stool consistency. ORS, with or without antibiotics, is the current standard of care for infectious diarrhea. NP-300 provides a first-of-its-kind antisecretory antidiarrheal drug that would potentially reduce the duration of diarrhea, including its sequelae such as hospitalization.

#### **Manufacturing**

The plant material used to manufacture is crude plant latex ("CPL") extracted and purified from Croton lechleri, a widespread and naturally regenerating tree in the rainforest that is managed as part of sustainable harvesting programs. The tree is found in several South American countries and has been the focus of long-term sustainable harvesting research and development work. Napo's collaborating suppliers obtain CPL and arrange for the shipment of CPL to Napo's third-party contract manufacturer.

Napo's third-party contract manufacturer, India-based Glenmark Life Sciences Ltd. ("Glenmark"), a research-driven, global, integrated pharmaceutical company, is Napo's manufacturer of crofelemer, the active pharmaceutical ingredient in Mytesi. Glenmark processes CPL into crofelemer utilizing a proprietary manufacturing process. The processing occurs at an FDA-approved Glenmark facility. Additionally, Napo is establishing a second processing site, which will be operated by Indena S.p.A. ("Indena"), a Milan, Italy-based contract manufacturer dedicated to the identification, development, and production of high-quality active principles derived from plants, for use in the pharmaceutical, health food, and personal care industries. Indena has completed the required validation activities to gain approval as a manufacturer of crofelemer drug substance.

As announced January 25, 2023, the required procedure of registering the source of the API of crofelemer with the Agenzia Italiana Del Farmaco ("AIFA"), the Italian Medicines Agency, has been successfully completed. Resultingly, batches of crofelemer API manufactured by Indena can now be used by Jaguar for further development work. This was a key milestone in the ongoing process of establishing Indena as an additional approved crofelemer manufacturer as we work to support the increased crofelemer manufacturing demand expected upon potential FDA approval of crofelemer for new indications, including approval for CTD.

#### **Proprietary Library of Medicinal Plants**

We possess a proprietary library of more than 2,300 medicinal plants.

#### **Intellectual Property**

##### **Trademarks**

We plan to market all of our products under a trademark or trademarks we select, and we will own all rights, title and interest, including all goodwill, associated with such trademarks. Mytesi is a registered trademark owned by Napo. Jaguar Animal Health is a trademark owned by Jaguar.

## **License Agreements**

### **Patent Portfolio**

#### **Napo**

Napo owns a portfolio of patents and patent applications covering formulations of and treatment methods with proanthocyanidin polymers isolated from *Croton* spp. or *Calophyllum* spp., including Mytesi (crofelemer).

Napo owns a family of patents arising from International Patent Application Publication WO2012/058664 that cover methods of treating HIV-associated diarrhea and Highly Active Antiretroviral Therapy “HAART” associated diarrhea with proanthocyanidin polymers isolated from *Croton* spp. or *Calophyllum* spp., including crofelemer. In the US, there are two issued patents, US 8,962,680 and US 9,585,868, both of which expire on October 31, 2031. Outside the US, patent protection for methods of treating HIV-associated diarrhea has been obtained in Australia, Europe, Hong Kong, Japan, Kenya, Mexico, Russia, Ukraine, South Africa, and Zimbabwe, with expiration dates of October 31, 2031, and applications are pending in Brazil, Hong Kong, and China. Napo also has patent families related to methods of treating diarrhea-predominant irritable bowel syndrome, methods of treating constipation-predominant irritable bowel syndrome, and methods of treating inflammatory bowel disease, familial adenomatous polyposis, and colon cancer, with proanthocyanidin polymers isolated from *Croton* spp. or *Calophyllum* spp., including crofelemer. In particular, for diarrhea predominant irritable bowel syndrome, Napo has two issued US patents, US 8,846,113 and US 9,980,938, which expire on February 9, 2027, as well as issued patents in Australia, Canada, Europe, Gulf States, Hong Kong, Japan, South Korea, Mexico, New Zealand, Singapore, Thailand, and Taiwan and pending applications in Bangladesh, and Venezuela, all of which are estimated to expire April 30, 2027; for constipation predominant irritable bowel syndrome, Napo has three issued US patents, with terms to at least April 30, 2027, patents in Australia, Canada, Europe, Hong Kong, Mexico, New Zealand, and Singapore, all of which are estimated to expire April 30, 2027; and for inflammatory bowel disease, familial adenomatous polyposis and/or colon cancer, Napo has two issued US patents, US 8,852,649 and US 9,987,250 with terms until at least January 4, 2028, as well as issued patents in Australia, Hong Kong, and Europe and Canada, which have estimated expiration dates of April 30, 2027. Napo has a US patent for the treatment of CID caused by neratinib with crofelemer and a related continuation application also directed to treating CID effectively filed on March 9, 2018, as well as multiple pending national stage applications outside the US also directed to treating CID with crofelemer effectively filed June 19, 2020. In addition, Napo has two patent families, each with pending applications in the US, Australia, Canada, China, Europe, Israel, Jordan, Japan, and the Gulf States, directed to the treatments of SBS and CDD, respectively, and each filed on May 31, 2018. Napo also has pending international applications to “Methods and Compositions for Treating Post-Acute Infection Gastrointestinal Disorders,” filed November 23, 2021.

For methods of manufacturing proanthocyanidin polymers isolated from *Croton* spp. or *Calophyllum* spp., including crofelemer, Napo owns issued patents in India, South Africa, and Eurasia with terms at least until August 26, 2029. Napo also owns issued patents in Brazil, India, and Russia, and a pending application in Venezuela that also covers methods of manufacturing proanthocyanidin polymers isolated from *Croton* spp. or *Calophyllum* spp., including crofelemer, with terms at least until January 17, 2032. Lastly, Napo owns two US patents covering a formulation of NP 500 (nordihydroguiaretic acid (“NDGA”)) and its use in treating a metabolic disorder that has terms until April 23, 2031.

Napo also has two international applications pending directed to alstonine derivatives and salts thereof and uses thereof for treating psychotic disorders filed on June 14, 2022, and October 26, 2022, respectively.

#### **Napo grants license to Napo Therapeutics**

In August 2021, Napo signed a license agreement with Napo Therapeutics to study, develop, manufacture, and commercialize Napo’s plant-based crofelemer and NP-300 drug product candidates in the European Union (excluding Russia) and in specified non-EU countries in Europe for specific indications, which rights and obligations were assumed by the combined company formed by the merger of Napo EU S.p.A. with Dragon SPAC (the combined

company uses the Napo Therapeutics name). The license agreement grants Napo Therapeutics the rights for SBS-IF, HIV-related diarrhea, and the symptomatic relief and treatment of IF-related diarrhea in patients with congenital disorders.

#### **Government Regulation**

The FDA and comparable regulatory authorities in state and local jurisdictions and in other countries impose substantial and burdensome requirements upon companies involved in the clinical development, manufacture, marketing, and distribution of prescription drugs such as those Napo is that Jaguar and its subsidiaries are commercializing and/or developing. These agencies and other federal, state, and local entities regulate, among other things, the research and development, testing, manufacture, quality control, safety, effectiveness, labeling, storage, record keeping, approval, advertising and promotion, distribution, post-approval monitoring and reporting, sampling and export and import of Napo's drug product candidates. To comply with the regulatory requirements in each of the jurisdictions in which Napo is seeking to market and subsequently sell its prescription products, Napo has established processes and resources to provide oversight of the development, approval processes, and launch of its products and to position those products to gain market share.

##### ***US Government Regulation***

###### *Human Prescription Drugs*

In the US, the FDA approves and regulates drugs under the Federal Food, Drug, and Cosmetic Act ("FDCA") and its implementing regulations.

The process of obtaining regulatory approvals and the subsequent compliance with applicable federal, state, local, and foreign statutes and regulations requires substantial time and financial resources. Failure to comply with the applicable US requirements at any time during the product development process, approval process, or after approval may subject an applicant to a variety of administrative or judicial sanctions, such as the FDA's refusal to approve pending New Drug Applications ("NDAs"), withdrawal of an approval, imposition of a clinical hold, issuance of warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement or civil or criminal penalties.

The process required by the FDA before a human prescription drug may be marketed in the US generally involves the following:

- completion of pre-clinical laboratory tests, animal studies, and formulation studies in compliance with the FDA's good laboratory practice or good laboratory practices ("GLPs") regulations;
- submission to the FDA of an IND for human clinical trials;
- approval by an institutional review board ("IRB") for human trials. Multiple sites may necessitate the involvement of multiple IRBs and submissions for human health products;
- performance of adequate and well-controlled human clinical trials in accordance with good clinical practices ("GCPs"), requirements to establish the safety and efficacy of the proposed drug product for each indication;
- submission to the FDA of an NDA for marketing approval of human prescription drugs;
- satisfactory completion of FDA advisory committees review, if applicable;
- satisfactory completion of an FDA pre-approval inspection ("PAI") of the manufacturing facility or facilities at which the product is produced to assess compliance with current good manufacturing

practices ("cGMPs"), requirements and to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity; and

- FDA review and approval of the NDA.

*Pre-clinical Studies*

Pre-clinical studies include laboratory evaluation of the drug product's chemistry, toxicity, and formulation and animal studies to assess potential safety and effectiveness. An IND sponsor must submit the results of the pre-clinical tests, manufacturing information, analytical data, and any available clinical data or literature, among other things, to the FDA as part of an IND. Some pre-clinical testing may continue even after the IND is submitted. An IND automatically becomes effective 30 days after receipt by the FDA unless, before that time, the FDA raises concerns or questions about one or more proposed clinical trials and places the clinical trial on a clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, submission of an IND may not result in the FDA allowing clinical trials to commence.

*Clinical Trials for Human Prescription Drugs*

Clinical trials involve the administration of the investigational new drug to human subjects pursuant to a clinical protocol under the supervision of qualified investigators in accordance with GCPs requirements, which include the requirement that all research subjects provide their informed consent in writing for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives or endpoints of the trial, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA under the IND. In addition, an IRB at each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution. Information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health, or NIH, for public dissemination on their [www.clinicaltrials.gov](http://www.clinicaltrials.gov) website.

Human clinical trials are typically conducted in three sequential phases, which may overlap or be combined:

- Phase 1: The drug is initially introduced into healthy human subjects or patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion, and, if possible, to gain an early indication of its effectiveness depending on the endpoints set forth in the protocol.
- Phase 2: The drug is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.
- Phase 3: The drug is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to statistically evaluate the efficacy and safety of the product for approval, to establish the overall risk-benefit profile of the product, and to provide adequate information for the labeling of the product.

Progress reports detailing the results of the clinical trials must be submitted to the FDA at least annually and more frequently if serious adverse events occur. Phase 1, Phase 2, and Phase 3 clinical trials may not be completed successfully within any specified period or at all. Furthermore, the FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients.

*Special Protocol Assessment for Human Health Prescription Drugs*

The special protocol assessment ("SPA") process is designed to facilitate the FDA's review and approval of drugs by allowing the FDA to evaluate issues related to the adequacy of certain clinical trials, including Phase 3 clinical trials that can form the primary basis for a drug product's efficacy claim in an NDA. Upon specific request by a clinical trial sponsor, the FDA will evaluate the protocol and respond to a sponsor's questions regarding, among other things, primary efficacy endpoints, trial conduct, and data analysis within 45 days of receipt of the request.

The FDA ultimately assesses whether the protocol design and planned analysis of the trial are acceptable to support regulatory approval of the product candidate with respect to the effectiveness of the indication studied. All agreements and disagreements between the FDA and the sponsor regarding an SPA must be clearly documented in an SPA letter or meeting minutes between the sponsor and the FDA.

Even if the FDA agrees to the design, execution, and analyses proposed in protocols reviewed under the SPA process, the FDA may revoke or alter its agreement under the following circumstances:

- public health concerns emerge that were unrecognized at the time of the protocol assessment;
- the director of the review division determines that a substantial scientific issue essential to determining safety or efficacy has been identified after testing has begun;
- a sponsor fails to follow a protocol that was agreed upon with the FDA; or
- the relevant data, assumptions, or information provided by the sponsor in a request for SPA change, are found to be false statements or misstatements or are found to omit relevant facts.

A documented SPA may be modified, and such modification will be deemed binding on the FDA review division, except under the circumstances described above, if the FDA and the sponsor agree in writing to modify the protocol and such modification is intended to improve the study.

*Marketing Approval for Human Prescription Drugs*

Assuming successful completion of the required clinical testing, the results of the pre-clinical studies and clinical trials, together with detailed information relating to the product's chemistry, manufacture, controls, and proposed labeling, among other things, are submitted to the FDA as part of an NDA requesting approval to market the product for one or more indications. In most cases, submitting an NDA is subject to a substantial application user fee. Under the Prescription Drug User Fee Act ("PDUFA") guidelines that are currently in effect, the FDA has a goal of ten months from the date of "filing" of a standard NDA for a new molecular entity to review and act on the submission. This review typically takes twelve months from the date the NDA is submitted to the FDA because the FDA has approximately two months to make a "filing" decision.

In addition, under the Pediatric Research Equity Act of 2003, as amended and reauthorized, certain NDAs or supplements to an NDA must contain data that are adequate to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations; this would include information which supports dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults or full or partial waivers from the pediatric data requirements.

The FDA may also require the submission of a risk evaluation and mitigation strategy ("REMS"), plan to ensure that the drug's benefits outweigh its risks. The REMS plan could include medication guides, physician communication plans, assessment plans, and/or elements to assure safe use, such as restricted distribution methods, patient registries, or other risk minimization tools.

The FDA may also require other information as part of the NDA filing, such as an environmental impact statement. The FDA can waive some or delay compliance with some of these requirements.

The FDA conducts a preliminary review of all NDAs within the first 60 days after submission before accepting them for filing to determine whether they are sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. The FDA begins an in-depth substantive review once the submission is accepted for filing. The FDA reviews an NDA to determine, among other things, whether the drug is safe and effective and whether the facility in which it is manufactured, processed, packaged, or held meets standards designed to assure the product's continued safety, quality, and purity.

The FDA may refer an application for a novel drug to an advisory committee. An advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates, and recommends whether the application should be approved and under what conditions. The recommendations of an advisory committee do not bind the FDA, but it considers such recommendations carefully when making decisions.

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities comply with cGMPs requirements and are adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA may inspect one or more clinical trial sites to ensure compliance with GCPs requirements.

After evaluating the NDA and all related information, including the advisory committee recommendation, if any, and inspection reports regarding the manufacturing facilities and clinical trial sites, the FDA may issue an approval letter or, in some cases, a complete response letter. A complete response letter must contain a statement of specific items that prevent the FDA from approving the application and will also contain conditions that must be met to secure final approval of the NDA and may require additional clinical or pre-clinical testing for the FDA to reconsider the application. Even with the submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. If and when those conditions have been met to the FDA's satisfaction, the FDA will typically issue an approval letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications.

Even if the FDA approves a product, it may limit the approved indications for use of the product, require that contraindications, warnings, or precautions be included in the product labeling, require that post-approval studies, Phase 4 clinical trials, be conducted to further assess a drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution and use restrictions or other risk management mechanisms under a REMS, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-marketing studies or surveillance programs. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes, and additional labeling claims, are subject to further testing requirements and FDA review and approval.

#### *Post-Approval Requirements for Human Prescription Drugs*

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising, and promotion, and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. Clinical trials or data must support new secondary indications. There are also continuing annual user fee requirements for any marketed products and the establishments at which such products are manufactured, as well as new application fees for supplemental applications with clinical data.

The FDA may impose a number of post-approval requirements as a condition for approval of an NDA. For example, the FDA may require post-marketing testing, including Phase 4 clinical trials and surveillance to further assess and monitor the product's safety and effectiveness after commercialization.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMPs requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP requirements and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may use. Accordingly, manufacturers must continue to expend time, money, and effort in production and quality control to maintain cGMP compliance.

Once approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in mandatory revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, include, but are not limited to:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability. In addition, the FDA regulates the purity and or consistency of the approved product. Products, if deemed adulterated, can lead to serious consequences, as set forth above as well as civil and criminal penalties.

#### ***EMA Regulation of Human Prescription Drugs***

Napo and Napo Therapeutics intend to leverage the orphan medicines marketing authorization incentives from the EMA for the SBS and CDD indications for crofelemer for the licensed territories in the European Union. EMA has developed a regulatory procedure for sponsor eligibility for incentives available for drugs with ODD for the appropriate patient populations in an expedited manner. The EMA is responsible for scientific evaluation of centralized marketing authorization applications ("MAA"). Once granted by the European Commission, the centralized MAA is valid in all EU member states, Iceland, Norway, and Liechtenstein.

#### ***Centralized authorization procedure***

Under the centralized authorization procedure, pharmaceutical companies submit a single marketing authorization application to EMA. This allows the marketing-authorization holder to market the medicine and make it available to patients and healthcare professionals throughout the EU on the basis of a single marketing authorization.

EMA's Committee for Medicinal products for Human Use ("CHMP") or Committee for Medicinal products for Veterinary Use ("CVMP") carry out a scientific assessment of the application and give a recommendation on whether the medicine should be marketed or not. However, under EU law EMA has no authority to actually permit

marketing in the different EU countries. The European Commission is the authorizing body for all centrally authorized product, who takes a legally binding decision based on EMA's recommendation. This decision is issued within 67 days of receipt of EMA's recommendation.

Once granted by the European Commission, the centralized marketing authorization is valid in all EU Member States as well as in the European Economic Area ("EEA") countries Iceland, Liechtenstein, and Norway. Commission decisions are published in the Community Register of Medicinal Products for human use.

Centralized Procedure is mandatory for certain types of products, such as biotechnology medicinal products, orphan medicinal products, and medicinal products containing a new active substance indicated for the treatment of AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and viral diseases.

***Conditional marketing authorization***

The EMA supports the development of medicines that address unmet medical needs. In the interest of public health, applicants may be granted conditional marketing authorization for such medicines on less comprehensive clinical data than normally required, where the benefit of immediate availability of the medicine outweighs the risk inherent in the fact that additional data are still required.

Medicines for human use are eligible if they are intended for treating, preventing, or diagnosing seriously debilitating or life-threatening diseases. This includes orphan medicines. Its use is also intended for a public health emergency (e.g., a pandemic). For these medicines, less comprehensive pharmaceutical and non-clinical data may also be accepted. The legal basis is Article 14-a of Regulation (EC) No 726/2004. The provisions for granting a conditional marketing authorization are further elaborated in Regulation (EC) No 507/2006.

***Criteria and conditions***

EMA's CHMP may grant conditional marketing authorization for medicine if it finds that all of the following criteria are met:

- the benefit-risk balance of the medicine is positive;
- it is likely that the applicant will be able to provide comprehensive data post-authorization;
- the medicine fulfills an unmet medical need; and
- the benefit of the medicine's immediate availability to patients is greater than the risk inherent in requiring additional data.

Conditional marketing authorizations are valid for one year and can be renewed annually. Once a conditional marketing authorization has been granted, the marketing authorization holder must fulfill specific obligations within defined timelines. These obligations could include completing ongoing or new studies or collecting additional data to confirm the medicine's benefit-risk balance remains positive. EMA publishes the conditions of the marketing authorization in the medicine's European public assessment report.

The marketing authorization can be converted into a standard marketing authorization (no longer subject to specific obligations) once the marketing authorization holder fulfills the obligations imposed and the complete data confirms that the medicine's benefits continue to outweigh its risks. Initially, this is valid for five years. It can then be renewed for unlimited validity.

As for any medicine, if new data show that the medicine's benefits no longer outweigh its risks, EMA can take regulatory action, such as suspending or revoking the marketing authorization. EMA can also take regulatory action if the company does not comply with the imposed obligations.

Despite earlier approval, it guarantees that the medicine meets rigorous EU safety, efficacy and quality standards and that comprehensive data is still generated post-approval. It offers a robust post-authorization regulatory framework based on legally binding obligations, safeguards, and controls.

These include:

- full prescribing information and package leaflet with detailed instructions for safe use and conditions for storage;
- a robust risk-management and safety monitoring plan;
- manufacturing controls, including official batch controls for vaccines, as required;
- legally binding post-approval obligations (i.e., conditions) for the marketing authorization holder and a clear legal framework for the evaluation of emerging efficacy and safety data;
- a pediatric investigation plan.

***Guidance for applicants for conditional marketing authorization***

EMA advises applicants to discuss their development plans with the EMA via scientific advice or protocol assistance early in the development process. Early involvement of health technology assessment bodies is also encouraged, which is possible via EMA's parallel consultations procedure. The applicant should indicate a request for conditional marketing authorization in their notification of intention to submit a marketing authorization application. They should submit this six to seven months before submitting the application. EMA also encourages applicants to discuss their plans further with EMA as part of a pre-submission meeting. For products deemed suitable for conditional marketing authorization, EMA also encourages applicants to consider requesting accelerated assessment.

Applicants should include a formal request for a conditional marketing authorization in their marketing authorization application. The CHMP will assess this request together with the application. Guideline on the scientific application and the practical arrangements necessary to implement Regulation (EC) No 507/2006 on the conditional marketing authorization for medicinal products for human use falling within the scope of Regulation (EC) No 726/2004.

***Distinction from authorization under exceptional circumstances***

EMA may also grant marketing authorization in the absence of comprehensive data under exceptional circumstances. Unlike conditional marketing authorization, where marketing approval is granted in the likelihood that the sponsor will provide such data within an agreed timeframe, EMA can grant authorization under exceptional circumstances when comprehensive data cannot be obtained even after authorization. This authorization route normally does not lead to a standard marketing authorization.

**Orphan drug development incentives from EMA**

***Protocol assistance***

The EMA provides a form of scientific advice specifically for orphan medicines called protocol assistance. This allows sponsors to get answers to their questions on the types of studies needed to demonstrate the medicine's quality, benefits, and risks, as well as information on the significant benefit of the medicine. Protocol assistance is available at a reduced charge for designated orphan medicines, linked to a fee-reduction scale that depends on the sponsor's status. There is no restriction on the number of times a sponsor can request protocol assistance.

The EMA encourages sponsors to consider coordinating the timing of protocol assistance from the EMA with the request for scientific advice from the FDA. Parallel scientific advice with the FDA is available.

#### ***Access to the centralized authorization procedure***

All designated orphan medicines are assessed for central marketing authorization in the European Union. This allows companies to make a single application to the EMA, resulting in a single opinion and a single decision from the European Commission, valid in all EU Member States. Sponsors may also have access via orphan designation to conditional approval, which is conducted under the centralized procedure.

#### ***Ten years of market exclusivity***

Once approved, authorized orphan medicines benefit from ten years of protection from market competition with similar medicines with similar indications. This protection period is extended by two years for medicines that also have complied with an agreed pediatric investigation plan granted at the time of review of the orphan medicine designation.

#### ***Additional incentives for micro, small and medium-sized enterprises (“SMEs”)***

Companies classified as SMEs benefit from further incentives when developing medicines with orphan designation. These include administrative and procedural assistance from the EMA's SME office and fee reductions.

#### ***Fee reductions***

Companies applying for designated orphan medicines pay reduced fees for regulatory activities. This includes reduced fees for protocol assistance, marketing authorization applications, inspections before authorization, applications for changes to marketing authorizations made after approval, and reduced annual fees. Fee reductions are revised each year in relation to the budget available.

#### ***EMA Grants***

The EMA does not offer research grants for sponsors of orphan medicines, but funding is available from the European Commission and other sources:

- Horizon 2020, the EU Framework Programme for Research and Innovation;
- E-Rare, a transnational project for research programs on rare diseases
- Grants are also available for sponsors considering research in the US or Japan:
- US: Food and Drug Administration: Orphan products grants program
- Japan: National Institute of Biomedical Innovation: Services to promote development of medicinal products for rare diseases

#### ***Incentives in Member States***

Details on incentives available for designated orphan medicines in EU Member States are available in the European Commission's Inventory of Union and Member State incentives to support research into and the development and availability of orphan medicinal products.

#### ***Activities after orphan designation***

The orphan designation makes the sponsor eligible for a number of orphan incentives. Sponsors need to comply with various activities that take place after a designation has been granted. Sponsors should submit all post-designation activities, including annual reports. For information and guidance on using IRIS, see the IRIS homepage. Sponsors must submit an annual report on development to the EMA summarizing the status of the development of the medicine.

Sponsors of medicines with orphan designation should also remember to apply for a pediatric investigation plan ("PIP"), deferral, or waiver at the appropriate time, as specified in the Pediatric regulation.

Sponsors also need to submit an application for maintenance of the orphan designation at the time of marketing authorization to be eligible for the ten-year market exclusivity incentive.

A valid and completed PIP could make the sponsor eligible for the two-year marketing exclusivity extension to the ten-year marketing exclusivity granted at the time of review of the orphan medicinal designation. Transfers of orphan designation from one sponsor to another are possible. Transfers are free of charge. Sponsors can also request removal of an orphan designation.

#### ***EMA Compassionate Use Program***

Compassionate use is a treatment option that allows the use of an unauthorized medicine. Under strict conditions, products in development can be made available to groups of patients who have a disease with no satisfactory authorized therapies and who cannot enter clinical trials. The EMA provides recommendations through CHMP but these do not create a legal framework. Compassionate use programs are coordinated and implemented by Member States, which set their own rules and procedures.

Established by Article 83 of Regulation (EC) No 726/2004, this tool is designed to:

- facilitate and improve access to compassionate use programs by patients in the EU;
- favor a common approach regarding the conditions of use, the conditions for distribution, and the patients targeted for the compassionate use of unauthorized new medicines;
- increase transparency between Member States in terms of treatment availability.

These programs are only put in place if the medicine is expected to help patients with life-threatening, long-lasting, or seriously debilitating illnesses that cannot be treated satisfactorily with any currently authorized medicine. The medicine must be undergoing clinical trials or have entered the marketing-authorization application process, and while early studies will generally have been completed, its safety profile and dosage guidelines may not be fully established.

#### ***How to request an opinion for Compassionate Use***

National competent authorities can ask EMA for an opinion on how to administer, distribute, and use certain medicines for compassionate use. The CHMP also identifies which patients would benefit, and Member States should take note of these recommendations when making decisions.

Manufacturers and marketing-authorization applicants should not contact the EMA to request an opinion, but they may wish to inform the EMA of applications underway at a national level. National competent authorities will inform the EMA if they are making a product available to a group of patients for compassionate use.

#### ***Comparison to individual basis treatment (Named Patient Program)***

Compassionate use should not be confused with 'named-patient basis' treatments, which see doctors obtain medicines directly from manufacturers before authorization. This is done on an individual basis under the direct responsibility of the doctor, and the EMA does not need to be informed.

In general, medicines that are not yet authorized are first made available through clinical trials, and patients should always be considered for inclusion in trials before being offered compassionate use programs.

### **Compassionate use recommendations**

EMA's recommendations cover how a medicine should be used in compassionate use programs across the EU, and the type of patient who may benefit from treatment. EMA does not update its recommendations after a medicine receives marketing authorization, as all relevant information on the medicine's use is available in its European Public Assessment Report ("EPAR"). However, compassionate use programs may continue in certain Member States until the medicine becomes available on the market.

### **Rewards and incentives for pediatric medicines**

Several rewards and incentives for the development of pediatric medicines for children are available in the EU. Medicines authorized across the EU with the results of studies from a pediatric investigation plan included in the product information are eligible for an extension of their supplementary protection certificate by six months. This is the case even when the studies' results are negative.

For orphan medicines, the incentive is an additional two years of market exclusivity.

Scientific advice and protocol assistance at the EMA are free of charge for questions relating to the development of pediatric medicines. Medicines developed specifically for children that are already authorized but are not protected by a patent or supplementary protection certificate are eligible for a pediatric-use marketing authorization ("PUMA"). If a PUMA is granted, the product will benefit from 10 years of market protection as an incentive. The above can be complemented by other incentives to support the research, development and availability of medicinal products for pediatric use.

### **Market exclusivity: Orphan medicines**

Orphan medicines benefit from ten years of market exclusivity once they receive marketing authorization in the EU. This measure is intended to encourage the development of medicines for rare diseases by protecting them from competition from similar medicines with similar indications, which cannot be marketed during the exclusivity period. Market exclusivity is an orphan incentive awarded by the European Commission to a specific clinical indication with an orphan designation.

Each indication with an orphan designation confers ten years of market exclusivity for the particular indication. A medicine that has multiple orphan designations for different conditions will benefit from separate market exclusivity periods pertaining to its different orphan designations.

To benefit from market exclusivity, a medicine must maintain its orphan designation at the time of marketing authorization.

### **Extension of market exclusivity period**

The market exclusivity period is extended by two additional years for an orphan-designated condition when the results of specific studies are reflected in the summary of product characteristics ("SmPC") addressing the pediatric population and completed in accordance with a fully compliant PIP.

The European Commission grants the extension based on a positive compliance check from the Pediatric Committee and opinion from the CHMP and includes this information in the Community register of orphan medicinal products.

### **Review of the market exclusivity period**

Article 8(2) of the Orphan Regulation establishes the possibility for Member States to request that the market exclusivity be reduced from ten to six years under certain circumstances.

#### **Expiry of market exclusivity**

When the period of market exclusivity for an indication ends, the orphan designation for that indication expires, and the European Commission removes it from the CHMP.

Once all of the orphan designations associated with an approved medicine have expired or been withdrawn by the sponsor, the medicine ceases to be classified as an orphan medicine and no longer benefits from the orphan incentives.

#### **European Union's new chemical entity exclusivity**

In the EU, new chemical entities, sometimes referred to as new active substances, qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity. This data exclusivity, if granted, prevents regulatory authorities in the European Union from referencing the innovator's data to assess a generic application for eight years, after which a generic marketing authorization application can be submitted, and the innovator's data may be referenced, but not approved for two years. The overall ten-year period will be extended to a maximum of 11 years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies.

#### **European Union orphan designation and exclusivity**

In the EU, the EMA's Committee for Orphan Medicinal Products grants ODD to promote the development of products that are intended for the diagnosis, prevention, or treatment of life-threatening or chronically debilitating conditions affecting not more than 5 in 10,000 persons in the European Union Community and for which no satisfactory method of diagnosis, prevention, or treatment has been authorized (or the product would be a significant benefit to those affected). Additionally, the designation is granted for products intended for the diagnosis, prevention, or treatment of a life-threatening, seriously debilitating, or serious and chronic condition and when, without incentives, it is unlikely that sales of the drug in the European Union would be sufficient to justify the necessary investment in developing the medicinal product.

In the European Union, ODD entitles a party to financial incentives such as reduction of fees or fee waivers, and ten years of market exclusivity is granted following medicinal product approval. This period may be reduced to six years if the ODD criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify the maintenance of market exclusivity. ODD must be requested before submitting an application for marketing approval. ODD does not convey any advantage in or shorten the duration of the regulatory review and approval process.

#### **European Union Pediatric Plan**

In the EEA, marketing authorization applications for new medicinal products not authorized have to include the results of studies conducted in the pediatric population, in compliance with a pediatric investigation plan, or PIP, agreed with the EMA's Pediatric Committee ("PDCO"). The PIP sets out the timing and measures proposed to generate data to support a pediatric indication of the drug for which marketing authorization is being sought. The PDCO can grant a deferral of the obligation to implement some or all of the measures of the PIP until there is sufficient data to demonstrate the efficacy and safety of the product in adults. Further, the obligation to provide pediatric clinical trial data can be waived by the PDCO when these data are not needed or appropriate because the product is likely to be ineffective or unsafe in children, the disease or condition for which the product is intended occurs only in adult populations, or when the product does not represent a significant therapeutic benefit over existing treatments for pediatric patients. Once the marketing authorization is obtained in all Member States of the EU and study results are included in the product information, even when negative, the product is eligible for six six-month supplementary protection certificate extension. For orphan drug-designated medicinal products, the 10-year period of market exclusivity is extended to 12 years.

### ***Clinical Trials Regulation in Europe***

In the EU, pursuant to the currently applicable Clinical Trials Directive 2001/20/EC and the Directive 2005/28/EC on GCP, a system for the approval of clinical trials in the EU has been implemented through national legislation of the EU member states. Under this system, an applicant must obtain approval from the national competent authority of an EU member state in which the clinical trial is to be conducted or in multiple member states if the clinical trial is to be conducted in a number of member states. Furthermore, the applicant may only start a clinical trial at a specific study site after the independent ethics committee for each site has issued a favorable opinion. The clinical trial application must be accompanied by an investigational medicinal product dossier with supporting information prescribed by Directive 2001/20/EC and Directive 2005/28/EC and corresponding national laws of the individual EU member states and further detailed in applicable guidance documents. In April 2014, the EU adopted a new Clinical Trials Regulation (EU) No 536/2014, which is set to replace the current Clinical Trials Directive 2001/20/EC. It is anticipated that the new Clinical Trials Regulation (EU) No 536/2014 may come into effect in late 2021 with a three-year transition period for some types of clinical trials. It will overhaul the current system of approvals for clinical trials in the EU. Specifically, the new regulation, which will be directly applicable in all EU member states, aims to simplify and streamline the approval of clinical trials in the EU. For instance, the new Clinical Trials Regulation provides for a streamlined application procedure via a single entry point and strictly defined deadlines for the assessment of clinical trial applications.

### ***Other US Healthcare Laws***

In addition to FDA restrictions on the marketing of pharmaceutical and biological products, other US federal and state healthcare regulatory laws restrict business practices in the pharmaceutical industry, which include, but are not limited to, state and federal anti-kickback, false claims, data privacy and security and physician payment and drug pricing transparency laws.

The US federal Anti-Kickback Statute prohibits, among other things, any person or entity from knowingly and willfully offering, paying, soliciting, receiving, or providing any remuneration, directly or indirectly, overtly or covertly, to induce or in return for purchasing, leasing, ordering, or arranging for or recommending the purchase, lease, or order of any good, facility, item or service reimbursable, in whole or in part, under Medicare, Medicaid or other federal healthcare programs. The term "remuneration" has been broadly interpreted to include anything of value. The Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers, formulary managers, and beneficiaries on the other. Although there are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution, the exceptions and safe harbors are drawn narrowly. Practices that involve remuneration that may be alleged to be intended to induce prescribing, purchases, or recommendations may be subject to scrutiny if they do not meet the requirements of a statutory or regulatory exception or safe harbor. Failure to meet all of the requirements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct *per se* illegal under the US federal Anti-Kickback Statute. Instead, the legality of the arrangement will be evaluated on a case-by-case basis based on a cumulative review of all its facts and circumstances. Several courts have interpreted the statute's intent requirement to mean that if any one purpose of an arrangement involving remuneration is to induce referrals of federal healthcare-covered business, the statute has been violated.

Additionally, the intent standard under the US federal Anti-Kickback Statute was amended by the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively, the ACA, to a stricter standard such that a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. In addition, the ACA codified case law that a claim including items or services resulting from a violation of the US federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal Civil False Claims Act. The majority of states also have Anti-Kickback laws, which establish similar prohibitions and, in some cases, may apply to items or services reimbursed by any third-party payer, including commercial insurers.

The federal false claims and civil monetary penalties laws, including the civil False Claims Act, prohibit any person or entity from, among other things, knowingly presenting, or causing to be presented, a false, fictitious, or

fraudulent claim for payment to, or approval by, the federal government, knowingly making, using, or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government, or from knowingly making a false statement to avoid, decrease or conceal an obligation to pay money to the US federal government. A claim includes "any request or demand" for money or property presented to the US government. Actions under the Civil False Claims Act may be brought by the Attorney General or as a qui tam action by a private individual in the name of the government. Violations of the Civil False Claims Act can result in very significant monetary penalties and triple damages. Several pharmaceutical and other healthcare companies have been prosecuted under these laws for, among other things, allegedly providing free products to customers with the expectation that the customers would bill federal programs for the product. Other companies have been prosecuted for causing false claims to be submitted because of the companies' marketing of products for unapproved or off-label uses. Companies have also been prosecuted for allegedly violating the Anti-Kickback Statute and False Claims Act as a result of impermissible arrangements between companies and healthcare practitioners or as a result of the provision of remuneration by the companies to healthcare practitioners. In addition, the civil monetary penalties statute imposes penalties against any person who is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent. Many states also have similar fraud and abuse statutes or regulations that apply to items and services reimbursed under Medicaid and other state programs or, in several states, apply regardless of the payer.

Violations of fraud and abuse laws, including federal and state Anti-Kickback and false claims laws, may be punishable by criminal and civil sanctions, including fines and civil monetary penalties, the possibility of exclusion from federal healthcare programs (including Medicare and Medicaid), disgorgement and corporate integrity agreements, which impose, among other things, rigorous operational and monitoring requirements on companies. Similar sanctions and penalties, as well as imprisonment, also can be imposed upon executive officers and employees of such companies. Given the significant size of actual and potential settlements, it is expected that the government authorities will continue to devote substantial resources to investigating healthcare providers' and manufacturers' compliance with applicable fraud and abuse laws.

The federal Health Insurance Portability and Accountability Act of 1996 ("HIPAA") created additional federal criminal statutes that prohibit, among other actions, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payers, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Similar to the US federal Anti-Kickback Statute, the ACA broadened the reach of certain criminal healthcare fraud statutes created under HIPAA by amending the intent requirement such that a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

In addition, there has been a recent trend of increased federal and state regulation of payments made to physicians and certain other healthcare providers. The ACA imposed, among other things, new annual reporting requirements through the Physician Payments Sunshine Act for covered manufacturers for certain payments and "transfers of value" provided to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Failure to submit timely, accurately, and completely the required information for all payments, transfers of value, and ownership or investment interests may result in civil monetary penalties of up to an aggregate of \$150,000 per year and up to an aggregate of \$1 million per year for "knowing failures." Covered manufacturers must submit reports by the 90th day of each subsequent calendar year. In addition, certain states require the implementation of compliance programs and compliance with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, impose restrictions on marketing practices and/or tracking and reporting of gifts, compensation and other remuneration or items of value provided to physicians and other healthcare professionals and entities.

Napo may also be subject to data privacy and security regulation by both the federal government and the states in which Napo conducts its business. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act ("HITECH"), and their respective implementing regulations, including the Final HIPAA

Omnibus Rule, published on January 25, 2013, impose specified requirements relating to privacy, security, and transmission of individually identifiable health information held by covered entities and their business associates. Among other things, HITECH made HIPAA's security standards directly applicable to "business associates," defined as independent contractors or agents of covered entities that create, receive, maintain, or transmit protected health information in connection with providing a service for or on behalf of a covered entity. HITECH also increased the civil and criminal penalties that may be imposed against covered entities, business associates, and possibly other persons and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorney's fees and costs associated with pursuing federal civil actions. In addition, state laws govern the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same requirements, thus complicating compliance efforts.

#### *Animal Health Prescription Drugs*

Under the FDCA, the term "drug" means articles recognized in the official US Pharmacopoeia, official Homeopathic Pharmacopoeia of the United States, or official National Formulary; articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals; and articles other than food intended to affect the structure or any function of the body of man or other animals. It also includes articles intended for use as a component of a drug.

Once a product is determined to be a drug for animal use, the next step is to determine whether or not it is a new animal drug. The FDCA defines a new animal drug (in part) as any drug intended for use for animals other than man, the composition of which is not generally recognized among experts qualified by scientific training and experience, as safe and effective for use under the conditions prescribed, recommended, or suggested in its labeling. By virtue of Supreme Court interpretations of the necessary basis for general recognition, there are, for all practical purposes, no animal drugs, which are not also new animal drugs.

Under the FDCA, a new animal drug may not be legally introduced into interstate commerce unless it is the subject of either:

- an approved New Animal Drug Application ("NADA") or abbreviated new animal drug application ("ANADA") under section 512 of the Act;
- a conditional approval under section 571 of the FDCA;
- a listing on the Legally Marketed Unapproved New Animal Drug Index for Minor Species (the "Index") under section 572 of the FDCA;
- an emergency use authorization ("EUA") under section 564 of the FDCA (an EUA may only be issued under very limited circumstances, more information regarding EUAs is available at this webpage: Emergency Use Authorization) ; or
- an investigational exemption under section 512(j) of the FDCA.

#### *Three Regulatory Pathways in the US to Legal Marketing Status for Animal Health Drugs*

##### **Approval**

An approved animal drug has gone through the NADA process or the ANADA process for an approved generic animal drug. If the information in the application meets the requirements for approval, FDA approves the animal drug. FDA's approval means the drug is safe and effective when it is used according to the label. FDA's approval also ensures that the drug's strength, quality, and purity are consistent from batch to batch and that the drug's labeling is truthful, complete, and not misleading.

### **Conditional Approval**

Conditional approval is only available for some animal drugs for use in a minor species or in a major species under special circumstances. A conditionally approved animal drug has gone through the FDA's approval process, but the drug has not yet met the effectiveness standard for full approval. FDA's conditional approval means that when used according to the label, the drug is safe and has a "reasonable expectation of effectiveness." FDA's conditional approval also means that the drug is properly manufactured.

The conditional approval is valid for one year. The drug company can ask the FDA to renew the conditional approval annually for up to four more years, for a total of five years of conditional approval. During the 5-year period, the drug company can legally sell the animal drug while collecting the remaining effectiveness data. After collecting the remaining effectiveness data, the company submits an application to the FDA for full approval. The agency reviews the application and, if appropriate, fully approves the drug.

### **Indexing**

An indexed animal drug is a drug on the FDA's Index of Legally Marketed Unapproved New Animal Drugs for Minor Species, referred to simply as "the Index." As the name says, a drug listed on the Index is unapproved but has legal marketing status. It can be legally sold for a specific use in certain minor species. Indexing is allowed for drugs for:

- Non-food-producing minor species, such as pet birds, hamsters, and ornamental fish. These animals are typically not eaten by people or by other animals that produce food for people to eat, and
- An early non-food life stage of a food-producing minor species, such as oyster spat (immature oysters). Because people do not generally eat oyster spat, a drug to treat a disease in spat can be indexed, but a drug to treat a disease in adult oysters, which people commonly eat, cannot be indexed.

Indexing a drug is quite different from the drug approval process. Indexing relies heavily on a panel of qualified experts outside the FDA. The experts review the drug's safety in the specific minor species and the drug's effectiveness for the intended use. All experts on the panel must agree that, when used according to the label, the drug's benefits outweigh the risks to the treated animal. If the FDA agrees with the panel, the agency adds the drug to the Index.

### **Animal Health Business Regulations**

The development, approval and sale of animal health products are governed by the laws and regulations of each country in which we intend to seek approval, where necessary, to market and subsequently sell our prescription drug and non-drug products. To comply with these regulatory requirements, we have established processes and resources to provide oversight of the development, approval processes, and launch of our products and to position those products in order to gain market share in each respective market.

Certain US federal regulatory agencies are charged with oversight and regulatory authority of animal health products in the US. These agencies, depending on the product and its intended use, may include the FDA, the USDA, and the Environmental Protection Agency. The approval of prescription drugs intended for animal use is regulated by the FDA's CVM. In addition, the Drug Enforcement Administration regulates animal therapeutics that are classified as controlled substances. In addition, the Federal Trade Commission may, in the case of non-drug products, regulate the marketing and advertising claims being made.

### **Labeling**

The FDA plays a significant role in regulating the labeling, advertising, and promotion of animal drugs. This is also true of regulatory agencies in the EU and other territories. In addition, advertising and promotion of animal health products are controlled by regulations in many countries. These rules generally restrict advertising and promotion to those claims and uses that have been reviewed and approved by the applicable agency. We will conduct

a review of advertising and promotional material for compliance with the local and regional requirements in the markets where we sell our product candidates.

**Coverage and Reimbursement**

Significant uncertainty exists as to the coverage and reimbursement status of any pharmaceutical products for which Napo obtains regulatory approval. In the US and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payers to reimburse all or part of the associated healthcare costs. Patients are unlikely to use Napo's products unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of Napo's products. Sales of any products for which Napo receives regulatory approval for commercial sale will, therefore, depend, in part, on the availability of coverage and adequate reimbursement from third-party payers. Third-party payers include government authorities, managed care plans, private health insurers, and other organizations. In the US, the process for determining whether a third-party payer will provide coverage for a pharmaceutical or biological product typically is separate from the process for setting the price of such product or for establishing the reimbursement rate that the payer will pay for the product once coverage is approved. Third-party payers may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the FDA-approved products for a particular indication. A decision by a third-party payer not to cover Napo's product candidates could reduce physician utilization of Napo's products once approved and have a material adverse effect on Napo's sales, results of operations, and financial condition. Moreover, a third-party payer's decision to provide coverage for a pharmaceutical or biological product does not imply that an adequate reimbursement rate will be approved. Adequate third-party reimbursement may not be available to enable Napo to maintain price levels sufficient to realize an appropriate return on Napo's investment in product development. Additionally, coverage and reimbursement for products can differ significantly from payer to payer. One third-party payer's decision to cover a particular medical product or service does not ensure that other payers will also provide coverage for the medical product or service or will provide coverage at an adequate reimbursement rate. As a result, the coverage determination process will require Napo to provide scientific and clinical support for the use of Napo's products to each payer separately, and it will be a time-consuming process.

In the EEA, governments influence the price of products through their pricing and reimbursement rules and control of national healthcare systems that fund a large part of the cost of those products to consumers. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed to by the government. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost-effectiveness of a particular product candidate to currently available therapies. Other member states allow companies to fix their own prices for medicines but monitor and control company profits. The downward pressure on health care costs in general, particularly prescription products, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross-border imports from low-priced markets exert commercial pressure on pricing within a country.

The containment of healthcare costs has become a priority of federal, state, and foreign governments, and the prices of pharmaceutical or biological products have been a focus in this effort. Third-party payers are increasingly challenging the prices charged for medical products and services, examining the medical necessity and reviewing the cost-effectiveness of pharmaceutical or biological products, medical devices, and medical services, in addition to questioning safety and efficacy. If these third-party payers do not consider Napo's products to be cost-effective compared to other available therapies, they may not cover Napo's products after FDA approval or if they do, the level of payment may not be sufficient to allow Napo to sell its products at a profit.

**Healthcare Reform**

A primary trend in the US healthcare industry and elsewhere is cost containment. Government authorities and other third-party payers have attempted to control costs by limiting coverage and the amount of reimbursement for particular medical products. For example, in March 2010, the ACA was enacted, which, among other things, increased the minimum Medicaid rebates owed by most manufacturers under the Medicaid Drug Rebate Program; introduced a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated

for drugs that are inhaled, infused, instilled, implanted or injected; extended the Medicaid Drug Rebate Program to the utilization of prescriptions of individuals enrolled in Medicaid managed care plans; imposed mandatory discounts for certain Medicare Part D beneficiaries as a condition for manufacturers' outpatient drugs covered under Medicare Part D; subjected drug manufacturers to new annual fees based on pharmaceutical companies' share of sales to federal healthcare programs; created a new Patient Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; creation of the Independent Payment Advisory Board, once empaneled, will have authority to recommend certain changes to the Medicare program that could result in reduced payments for prescription drugs; and establishment of a Center for Medicare Innovation at the CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending. Since its enactment, the US federal government has delayed or suspended the implementation of certain provisions of the ACA.

Napo expects that the ACA and other healthcare reform measures that may be adopted in the future may result in more rigorous coverage criteria, lower reimbursement, and additional downward pressure on the price that Napo receives for any approved product. Any reduction in reimbursement from Medicare or other government-funded programs may result in a similar reduction in payments from private payers. Moreover, recently, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products. The implementation of cost containment measures or other healthcare reforms may prevent Napo from being able to generate revenue, attain profitability or commercialize Napo's drugs.

Additionally, on August 2, 2011, the Budget Control Act of 2011 created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least \$1.2 trillion for the years 2013 through 2021, was unable to reach the required goals, thereby triggering the legislation's automatic reduction to several government programs. This included aggregate reductions of Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013, and due to subsequent legislative amendments to the statute, will stay in effect through 2025 unless additional action is taken by Congress. On January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several types of providers, including hospitals, imaging centers, and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. More recently, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which have resulted in several recent Congressional inquiries and proposed bills designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for pharmaceutical products.

Napo expects that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for Napo's products once approved or additional pricing pressures.

#### ***Other Regulatory Considerations***

We believe regulatory rules relating to human food safety, food additives, or drug residues in food will not apply to the products we currently are developing because our animal prescription drug product candidates are not intended for use in production animals, with the exception of horses, which qualify as food animals in Europe and Canada; and our nonprescription products are not regulated by section 201(g) of the Federal Food, Drug, and Cosmetic Act, which the FDA is authorized to administer.

We do not believe that our animal nonprescription products are currently subject to regulation in the US. The CVM only regulates those animal supplements that fall within the FDA's definition of an animal drug, food or feed additive. The Federal Food Drug and Cosmetic Act defines food as "articles used for food or drinks for man or other animals and articles used as components of any such article." Animal foods are not subject to pre-market approval and are designed to provide a nutritive purpose to the animals that receive them. Feed additives are defined as those articles that are added to an animal's feed or water, as illustrated by the guidance documents. Our nonprescription products are not added to food, are not ingredients in food, nor are they added to any animal's drinking water. There is

no intent to make our nonprescription products a component of animal food, either directly or indirectly. We do not believe that our nonprescription products fit the definition of an animal drug, food, or food additive and, therefore are not regulated by the FDA at this time.

In addition to the foregoing, we may be subject to state, federal, and foreign healthcare and/or veterinary medicine laws, including but not limited to anti-kickback laws, as we may, from time to time, enter consulting and other financial arrangements with veterinarians, who may prescribe or recommend our products. If our financial relationships with veterinarians are found to be in violation of such laws that apply to us, we may be subject to penalties.

#### **Legal Proceedings**

From time to time, we may become involved in litigation relating to claims arising from the ordinary course of business. Other than as set forth in "Item 3. LEGAL PROCEEDINGS", there are currently no claims or actions pending against us, the ultimate disposition of which could have a material adverse effect on our results of operations, financial condition, or cash flows.

#### **Corporate Information**

We were incorporated in the State of Delaware on June 6, 2013. Our principal executive office is located at 200 Pine Street, Suite 400, San Francisco, CA 94104, for human health prescription drugs, and the telephone number is (415) 371 8300. We have an additional office at 200 Pine Street, Suite 600, San Francisco, CA 94104, for Jaguar Animal Health. Our website for the corporation is <https://jaguar.health>. The information contained on, or that can be accessed through, our website is not part of this annual report. Our voting common stock is listed on the Nasdaq Capital Market and trades under the symbol "JAGX." On July 31, 2017, we completed the acquisition of Napo pursuant to the Agreement and Plan of Merger, dated March 31, 2017, by and among the Company, Napo, Napo Acquisition Corporation, and Napo's representative (the "Merger").

#### **Employees**

As of December 31, 2023, we had forty nine employees. Twelve employees hold M.D., D.V.M and/or Ph.D. degrees. Twenty-three of our employees are in research and development activities, and thirteen are in sales and marketing. We have four employees within Napo Therapeutics in Italy. Our employees are not represented by labor unions or covered by collective bargaining agreements.

#### **Description of Properties**

Our corporate headquarters are located in San Francisco, California, where we currently lease 10,526 rentable square feet of office space from M & E, LLC.

#### **ITEM 1A. RISK FACTORS**

The business, financial condition, and operating results of the Company may be affected by a number of factors, whether currently known or unknown, including but not limited to those described below. Any or more of such factors could directly or indirectly cause the Company's actual results of operations and financial condition to vary materially from past or anticipated future results of operations and financial condition. Any of these factors, in whole or in part, could materially and adversely affect the Company's business, financial condition, results of operations, and stock price. The following information should be read in conjunction with Part II, Item 7, "Management's Discussion and Analysis of Financial Condition and Results of Operations," and the consolidated financial statements and related notes in Part II, Item 8, "Financial Statements and Supplementary Data" of this Annual Report.

## Risk Factor Summary

The following is a summary of the principal risks that could adversely affect our business, operations, and financial results.

### **Risks Related to Our Business**

- We have a limited operating history, expect to incur further losses as we grow, and may be unable to achieve or sustain profitability.
- We expect to incur significant additional costs as we continue commercialization efforts for current prescription drug candidates or other product candidates and undertake the clinical trials necessary to obtain any necessary regulatory approvals, which will increase our losses.
- We will need to raise substantial additional capital in the future in the event that we conduct clinical trials for new indications, and we may be unable to raise such funds when needed and on acceptable terms, which would force us to delay, limit, reduce or terminate one or more of our product development programs.
- We are substantially dependent on the success of Mytesi, our current lead prescription drug product, and Canalevia-CA1, our conditionally approved prescription drug product for CID in dogs. We cannot be certain that necessary approvals will be received for planned Mytesi or Canalevia-CA1 follow-on indications or that these product candidates will be successfully commercialized by us or any of our partners.
- If we are not successful in identifying, licensing, developing, and commercializing additional product candidates and products, our ability to expand our business and achieve our strategic objectives could be impaired.
- Mytesi faces significant competition from other pharmaceutical companies, both for its currently approved indication and for planned follow-on indications, and our operating results will suffer if we fail to compete effectively.
- We may be unable to obtain, or obtain on a timely basis, regulatory approval for our existing or future human or animal prescription drug product candidates under applicable regulatory requirements, which would harm our operating results.
- The results of our earlier studies of Mytesi may not be predictive of the results in any future clinical trials and species-specific formulation studies, respectively, and we may not be successful in our efforts to develop or commercialize line extensions of Mytesi.
- Development of prescription drug products is inherently expensive, time-consuming, and uncertain, and any delay or discontinuance of our current or future pivotal trials would harm our business and prospects.
- We will partially rely on third parties to conduct our development activities. If these third parties do not successfully carry out their contractual duties, we may be unable to obtain regulatory approvals or commercialize our current or future human or animal product candidates on a timely basis or at all.
- Even if we obtain regulatory approval for planned follow-on indications of crofelemer, Canalevia, or our other product candidates, they may never achieve market acceptance. Further, even if we are successful in the ongoing commercialization of Mytesi and Canalevia, we may not achieve commercial success.
- Human and animal gastrointestinal health products are subject to unanticipated post-approval safety or efficacy concerns, which may harm our business and reputation.
- Future federal and state legislation may result in increased exposure to product liability claims, which could result in substantial losses.
- If we fail to retain current members of our senior management or to identify, attract, integrate, and retain additional key personnel, our business will be harmed.
- We are dependent on two suppliers for the raw material used to produce the active pharmaceutical ingredients in Mytesi and Canalevia. The termination of either of these contracts would result in a disruption to product development and harm our business.
- We are dependent upon third-party contract manufacturers, both for the supply of the active pharmaceutical ingredient in Mytesi and Canalevia-CA1, as well as for the supply of finished products for commercialization.
- If we are unable to establish sales capabilities on our own or through third parties, we may not be able to market and sell our current or future human products and product candidates, if approved, and generate product or other revenue.

- We will need to increase the size of our organization and may not successfully manage such growth.
- Canalevia-CA1 and our animal health prescription drug product candidates may be marketed in the US only in the target animals and for the indications for which they are approved, and if we want to expand the approved animals or indications, it will need to obtain additional approvals, which may not be granted.
- The misuse or extra-label use of Mytesi, Canalevia, and our human or animal prescription drug product candidates, if approved by regulatory authorities, may harm our reputation or result in financial or other damages.
- We may be unable to obtain, or obtain on a timely basis, a renewal of conditional approval for Canalevia-CA1 or to eventually obtain full regulatory approval of Canalevia-CA1, which would harm our operating results.
- We may not maintain the benefits associated with MUMS designation, including market exclusivity.
- The market for our human and animal products, and the gastrointestinal health market as a whole, is uncertain and may be smaller than we anticipate, which could lead to lower revenue and harm our operating results.
- Insurance coverage for Mytesi for its current approved indication could decrease or end, or Mytesi might not receive insurance coverage for any approved follow-on indications, which could lead to lower revenue and harm our operating results.
- We may engage in future acquisitions that increase our capital requirements, dilute our stockholders, cause us to incur debt or assume contingent liabilities, and subject us to other risks.
- Certain of the countries in which we plan to commercialize our products in the future are developing countries, some of which have potentially unstable political and economic climates.
- Fluctuations in the exchange rate of foreign currencies could result in currency transaction losses.
- Laws and regulations governing global trade compliance could adversely impact our business.
- There are other gastrointestinal-focused human pharmaceutical companies, and we face competition in the marketplaces in which we operate or plan to operate.
- Our obligations to Streeterville are secured by a security interest in all of Napo's NP-300 assets, so if we default on those obligations, Streeterville could foreclose on our assets.
- Our royalty interests require us to make minimum royalty payments, even if we do not sell a sufficient amount of products to cover the amount of such payments, which may strain our cash resources.
- Failure in our information technology systems, including by cyber-attacks or other data security incidents, could significantly disrupt our operations.
- Global macroeconomic conditions may negatively affect us and may magnify certain risks that affect our business.
- Unfavorable global economic conditions could adversely affect our business, financial condition, or results of operations.
- Substantially all of our revenue for recent periods has been received from two customers.
- The Company's ability to attract and retain qualified members of our board of directors may be impacted due to new state laws, including recently enacted gender quotas.
- Evolving expectations around corporate responsibility practices, specifically related to environmental, social, and governance ("ESG") matters, may expose us to reputational and other risks.
- The growing use of artificial intelligence ("AI") systems to automate processes, analyze data, and support decision-making poses inherent risks.

***Risks Related to Our Intellectual Property***

- We cannot be certain that our patent strategy will be effective in protecting against competition.
- Obtaining and maintaining our patent protection depends on compliance with various procedural requirements, document submission, fee payment, and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.
- Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, which would be costly and time-consuming and, if successfully asserted against us, delay or prevent the development and commercialization of our current or future products and product candidates.

- Our proprietary position depends upon the botanical guidance of our drug approval and patents that are formulation or method-of-use patents, which do not prevent a competitor from using the same human or animal drug for another use.
- We may be involved in lawsuits to protect or enforce our patents, which could be expensive, time-consuming, and unsuccessful, and third parties may challenge the validity or enforceability of our patents, and they may be successful.
- If we are unable to prevent disclosure of our trade secrets or other confidential information to third parties, our competitive position may be impaired.
- Changes in US patent law could diminish the value of patents in general, thereby impairing our ability to protect our products.
- We may not be able to protect our intellectual property rights throughout the world, which could impair our business.
- Our business could be harmed if we fail to obtain certain registered trademarks in the US or in other countries.
- We may be subject to claims that our employees, consultants, or independent contractors have wrongfully used or disclosed confidential third-party information.
- Even if we receive any of the required regulatory approvals for our current or future prescription drug product candidates and non-prescription products, we will be subject to ongoing obligations and continued regulatory review, which may result in significant additional expenses.
- Any of our current or future prescription drug product candidates or non-prescription products may cause or contribute to adverse medical events that we would be required to report to regulatory authorities and if we fail to do so, we could be subject to sanctions that would harm our business.
- Legislative or regulatory reforms with respect to animal health may make it more difficult and costly for us to obtain regulatory clearance or approval for any of our current or future product candidates and to produce, market, and distribute our products after clearance or approval is obtained.
- We believe that our non-prescription products are not subject to regulation by regulatory agencies in the US, but there is a risk that regulatory bodies may disagree with our interpretation or may redefine the scope of their regulatory reach in the future, which would result in additional expense and could delay or prevent the commercialization of these products.
- Even if we receive the required regulatory approvals for our current or future prescription drug product candidates and non-prescription products, we will be subject to ongoing obligations and continued regulatory review, which may result in significant additional expenses.

**Risks Related to Our Common Stock**

- Our failure to meet the continued listing requirements of The Nasdaq Capital Market could result in a delisting of our common stock.
- If our shares become subject to the penny stock rules, it would become more difficult to trade our shares.
- The price of our common stock could be subject to volatility related or unrelated to our operations, and purchasers of our common stock could incur substantial losses.
- A possible "short squeeze" due to a sudden increase in demand for our common stock that largely exceeds supply may lead to further price volatility in our common stock.
- You may be unable to resell our common stock when you wish to sell it or at a price that you consider attractive or satisfactory.
- If securities or industry analysts do not publish research or reports about our company, or if they issue adverse or misleading opinions regarding us or our stock, our stock price and trading volume could decline.
- You may be diluted by conversions of outstanding shares of non-voting common stock, exercises of outstanding options and warrants, and issuances of securities pursuant to our ATM Agreement.
- Provisions in our charter documents and under Delaware law could discourage a takeover that stockholders may consider favorable and may lead to entrenchment of management.
- Our amended and restated bylaws designate the Court of Chancery of the State of Delaware as the sole and exclusive forum for certain actions and proceedings that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or other employees.

- We do not intend to pay dividends on our common stock, and your ability to achieve a return on your investment will depend on appreciation in the market price of our common stock.
- The requirements of being a public company, including compliance with the reporting requirements of the Exchange Act and the requirements of the Sarbanes-Oxley Act, may strain our resources, increase our costs, and distract management, and we may be unable to comply with these requirements in a timely or cost-effective manner.
- We are a smaller reporting company, and the reduced reporting requirements applicable to smaller reporting companies may make our common stock less attractive to investors.

#### **Risks Related to Our Business**

***We have a limited operating history, expect to incur further losses as we grow, and may be unable to achieve or sustain profitability.***

Since the consummation of our merger with Napo Pharmaceuticals Inc. in 2017, our operations have been primarily focused on research, development, and the ongoing commercialization of our lead prescription drug product, Mytesi, which the FDA approves for the symptomatic relief of noninfectious diarrhea in adults with HIV/AIDS on antiretroviral therapy. As a result, we have limited meaningful historical operations upon which to evaluate our business and prospects and have not yet demonstrated an ability to broadly commercialize any of our human health products beyond Mytesi for HIV-related diarrhea or animal health products, obtain any required marketing approval for any of our animal prescription drug product candidates or successfully overcome the risks and uncertainties frequently encountered by companies in emerging fields such as the animal health industry or the gastrointestinal health industry in general. Our revenues to date have been insufficient to offset our expenses, and we expect to continue to incur significant research and development and other expenses. Our net comprehensive losses for the years ended December 31, 2023, and 2022 were \$41.9 million and \$49.1 million, respectively. As of December 31, 2023, we had a total stockholder equity of \$4.9 million. We expect to continue to incur losses for the foreseeable future, which will increase significantly from historical levels as we expand our product development activities, seek necessary approvals for our human and veterinary drug product candidates, conduct species-specific formulation studies for our non-prescription products, and increase commercialization activities. Even if we succeed in developing and broadly commercializing one or more of our products or product candidates, we expect to continue to incur losses for the foreseeable future, and we may never become profitable. If we fail to achieve or maintain profitability, then we may be unable to continue our operations at planned levels and be forced to reduce or cease operations.

As more fully discussed in Note 1 to our consolidated financial statements, we believe there is substantial doubt about our ability to continue as a going concern as we do not currently have sufficient cash resources to fund our operations through March 2025, or one year from the filing date of our Form 10-K. Our financial statements do not include any adjustments that may result from the outcome of this uncertainty. If we are unable to continue as a viable entity, our stockholders may lose their investment.

***We expect to incur significant additional costs as we continue commercialization efforts for current prescription drug candidates or other product candidates and undertake the clinical trials necessary to obtain any necessary regulatory approvals, which will increase our losses.***

Napo commenced sales of Mytesi for adults with HIV/AIDS on antiretroviral therapy in September 2016. Jaguar launched Canalevia-CA1 for chemotherapy-induced diarrhea (“CID”) in dogs in December 2021. We will need to continue to invest in developing our internal and third-party sales and distribution network and outreach efforts to key opinion leaders in the gastrointestinal health industry, including physicians and veterinarians, as applicable.

We are actively identifying additional products for development and commercialization and will continue to expend substantial resources for the foreseeable future to develop Mytesi, NP-300, and Canalevia-CA1. These expenditures will include costs associated with:

- identifying additional potential prescription drug product candidates and non-prescription products;

- formulation studies;
- conducting pilot, pivotal, and toxicology studies;
- completing other research and development activities;
- payments to technology licensors;
- maintaining our intellectual property;
- obtaining necessary regulatory approvals;
- establishing commercial supply capabilities and
- sales, marketing and distribution of our commercialized products.

We may also incur unanticipated costs in developing and commercializing our products. Because the outcome of our development activities and commercialization efforts is inherently uncertain, the actual amounts necessary to successfully complete the development and commercialization of our current or future products and product candidates may be greater than we anticipate.

Because we anticipate incurring significant costs for the foreseeable future, if we are not successful in broadly commercializing any of our current or future products or product candidates or raising additional funding to pursue our research and development efforts, we may never realize the benefit of our development efforts and our business may be harmed.

***In the event that we conduct clinical trials for new indications and new products, we will need to raise substantial additional capital in the future, and we may be unable to raise such funds when needed and on acceptable terms, which would force us to limit new indications and new product development.***

We are forecasting continued losses and negative cash flows as we continue to fund our operating and marketing activities and research and development programs and to complete the development of all the current products in our pipeline or any additional products we may identify. We will need to seek additional funds through public or private equity or debt financings or other sources such as strategic collaborations. Any such financings or collaborations may result in dilution to our stockholders, the imposition of debt covenants and repayment obligations, or other restrictions that may harm our business or the value of our common stock. We may also seek from time to time to raise additional capital based upon favorable market conditions or strategic considerations such as potential acquisitions or potential license arrangements.

Our future capital requirements depend on many factors, including, but not limited to:

- the scope, progress, results and costs of researching and developing our current and future prescription drug product candidates and non-prescription products;
- the timing of, and the costs involved in, obtaining any regulatory approvals for our current and any future products;
- the number and characteristics of the products we pursue;
- the cost of manufacturing our current and future products and any products we successfully commercialize;
- the cost of commercialization activities for Mytesi and Canalevia, if approved, including sales, marketing and distribution costs;
- the expenses needed to attract and retain skilled personnel;

- the costs associated with being a public company;
- our ability to establish and maintain strategic collaborations, distribution, or other arrangements and the financial terms of such agreements; and
- the costs involved in preparing, filing, prosecuting, maintaining, defending, and enforcing possible patent claims, including litigation costs and the outcome of any such litigation.

General economic conditions, both inside and outside the US, including heightened inflation, capital market volatility, interest rate and currency rate fluctuations, and economic slowdown or recession as well as the COVID-19 pandemic, including the evolution of new and existing variants of COVID-19, and geopolitical events, including civil or political unrest (such as the ongoing war between Ukraine and Russia), have resulted in a significant disruption of global financial markets. If the disruption persists and deepens, we could experience an inability to access additional capital, which could, in the future, negatively affect our capacity for certain corporate development transactions or our ability to make other important, opportunistic investments. In addition, market volatility, high levels of inflation, and interest rate fluctuations may increase our financing costs or restrict our access to potential sources of future liquidity. Additional funds may not be available when we need them on terms that are acceptable to us, or we may not have sufficient authorized shares to raise additional capital. If adequate funds are not available to us on a timely basis, we may be required to delay, limit, reduce, or terminate one or more of our product development programs or future commercialization efforts.

***We are substantially dependent on the success of Mytesi, our current lead prescription drug product, and Canalevia-CA1, our conditionally approved prescription drug product for CID in dogs. We cannot be certain that necessary approvals will be received for planned Mytesi and Canalevia-CA1 follow-on indications or that these product candidates will be successfully commercialized, either by us or any of our partners.***

Other than Mytesi and Canalevia-CA1 (for which we have conditional approval), we currently do not have regulatory approval for any of our prescription drug product candidates. Our current efforts are primarily focused on the ongoing commercialization of Mytesi and Canalevia-CA1 and development efforts related to Mytesi and Canalevia-CA1. With regard to Mytesi, we are focused on marketing the product in the US as well as on development efforts related to a follow-on indication for Mytesi in CTD, an important supportive care indication for patients undergoing primary or adjuvant chemotherapy for cancer treatment. Mytesi is also in development for other possible follow-up indications, including the rare disease indications of SBS with intestinal failure and CDD, for IBS-D and idiopathic/functional diarrhea, and for pediatric MVID patients. With regard to Canalevia-CA1, we are focused on the ongoing commercialization of the product in the US for CID in dogs. In addition, a second-generation proprietary anti-secretory agent is in development for symptomatic relief and treatment of moderate-to-severe diarrhea, with or without concomitant antimicrobial therapy, from bacterial, viral, and parasitic infections, including *Vibrio cholerae*, the bacterium that causes cholera. Crofelemer has been granted orphan-drug designation for SBS and MVID, a CDD condition, by both the FDA and EMA. Accordingly, our near-term prospects, including our ability to generate material product revenue, obtain any new financing if needed to fund our business and operations, or enter into potential strategic transactions, will depend heavily on the success of Mytesi and Canalevia-CA1.

Substantial time and capital resources have been previously devoted by third parties in the development of crofelemer, the active pharmaceutical ingredient ("API"), in Mytesi and Canalevia, and the development of the botanical extract used in Equilevia and Neonorm. Both crofelemer and the botanical extract used in Equilevia and Neonorm were originally developed at Shaman Pharmaceuticals, Inc. ("Shaman"), by certain members of our management team, including Lisa A. Conte, our chief executive officer and president, and Steven R. King, Ph.D., our executive vice president of sustainable supply, ethnobotanical research and intellectual property and secretary. Shaman spent significant development resources before voluntarily filing for bankruptcy in 2001 pursuant to Chapter 11 of the US Bankruptcy Code. The rights to crofelemer and the botanical extract used in Equilevia and Neonorm, as well as other intellectual property rights, were subsequently acquired by Napo from Shaman in 2001 pursuant to a court-approved sale of assets. Ms. Conte founded Napo in 2001 and was Napo's interim chief executive officer and a member of its board of directors prior to the merger. While at Napo, certain members of our management team, including Ms. Conte and Dr. King, continued the development of crofelemer. Following the merger of Jaguar and

Napo in July 2017, Napo became Jaguar's wholly-owned subsidiary. If we are not successful in the development and commercialization of Mytesi, our business, and our prospects will be harmed.

The successful development and commercialization of Mytesi and Canalevia-CA1 will depend on a number of factors, including the following:

- our ability to demonstrate, to the satisfaction of the FDA and any other regulatory bodies, the safety and efficacy of Canalevia;
- our ability and that of our contract manufacturers to manufacture supplies of Mytesi and Canalevia-CA1 and to develop, validate, and maintain viable commercial manufacturing processes that are compliant with current good manufacturing practices, or cGMPs if required;
- our ability to successfully market Mytesi and Canalevia-CA1, whether alone or in collaboration with others;
- the availability, perceived advantages, relative cost, relative safety, and relative efficacy of our prescription drug product candidates compared to alternative and competing treatments;
- the acceptance of our prescription drug product candidates and non-prescription products as safe and effective by physicians, veterinarians, patients, animal owners, and the human and animal health community, as applicable;
- our ability to achieve and maintain compliance with all regulatory requirements applicable to our business; and
- our ability to obtain and enforce our intellectual property rights and marketing exclusivity for our prescription drug product candidates and non-prescription products, and avoid or prevail in any third-party patent interference, patent infringement claims, or administrative patent proceedings initiated by third parties or the US Patent and Trademark Office ("USPTO").

Many of these factors are beyond our control. Accordingly, we may not be successful in developing or commercializing Mytesi, Neonorm, Equilevia, Canalevia, or any of our other potential products. If we are unsuccessful or are significantly delayed in commercializing Mytesi, our business and prospects will be harmed and you may lose all or a portion of the value of your investment in our common stock.

***If we are not successful in identifying, licensing, developing and commercializing additional product candidates and products, our ability to expand our business and achieve our strategic objectives could be impaired.***

Although a substantial amount of our efforts is focused on the commercial performance of Mytesi and Canalevia-CA1, a key element of our strategy is to identify, develop and commercialize a portfolio of products to serve the gastrointestinal health market. Most of our potential products are based on our knowledge of medicinal plants. Our current focus is primarily on product candidates whose active pharmaceutical ingredient or botanical extract has been successfully commercialized or demonstrated to be safe and effective in human or animal trials. In some instances, we may be unable to develop these potential products further because of perceived regulatory and commercial risks. Even if we successfully identify potential products, we may still fail to yield products for development and commercialization for many reasons, including the following:

- competitors may develop alternatives that render our potential products obsolete;
- an outside party may develop a cure for any disease state that is the target indication for any of our planned or approved drug products;

- potential products we seek to develop may be covered by third-party patents or other exclusive rights;
- a potential product may, on further study, be shown to have harmful side effects or other characteristics that indicate it is unlikely to be effective or otherwise does not meet applicable regulatory criteria;
- a potential product may not be capable of being produced in commercial quantities at an acceptable cost or at all; and
- a potential product may not be accepted as safe and effective by physicians, veterinarians, patients, animal owners, key opinion leaders, and other decision-makers in the gastrointestinal health market, as applicable.

While we are developing specific formulations, including flavors, methods of administration, new patents, and other strategies with respect to our current potential products, we may be unable to prevent competitors from developing substantially similar products and bringing those products to market earlier than we can. If such competing products achieve regulatory approval and commercialization prior to our potential products, our competitive position may be impaired. If we fail to develop and successfully commercialize other potential products, our business and future prospects may be harmed and we will be more vulnerable to any problems that we encounter in developing and commercializing our current potential products.

***Mytesi faces significant competition from other pharmaceutical companies, both for its currently approved indication and for planned follow-on indications, and our operating results will suffer if we fail to compete effectively.***

The development and commercialization of products for human gastrointestinal health is highly competitive, and our success depends on our ability to compete effectively with other products in the market. During the ongoing commercialization of Mytesi for its currently approved indication and during the future commercialization of Mytesi for any planned follow-on indications, if such follow-on indications receive regulatory approval, we expect to compete with major pharmaceutical and biotechnology companies that operate in the gastrointestinal space, such as Takeda Pharmaceuticals, Allergan, Inc., Ironwood Pharmaceuticals, Inc., Synergy Pharmaceuticals Inc., Sebela Pharmaceuticals, Inc., and Salix Pharmaceuticals.

Many of our competitors and potential competitors in the human gastrointestinal space have substantially more financial, technical, and human resources and a greater ability to lower manufacturing costs, sales and marketing costs than we do. Many also have more experience in developing, manufacturing, regulating, and commercializing human gastrointestinal health products worldwide.

For these reasons, we cannot be certain that we and Mytesi can compete effectively.

***We may be unable to obtain, or obtain on a timely basis, regulatory approval for our existing or future human or animal prescription drug product candidates under applicable regulatory requirements, which would harm our operating results.***

The research, testing, manufacturing, labeling, approval, sale, marketing and distribution of human and animal health products are subject to extensive regulation. We are typically not permitted to market our prescription drug product candidates in the US until we receive approval of the product from the FDA through the filing of an NDA or NADA, as applicable. To gain approval to market a prescription drug, we must provide the FDA with safety and efficacy data from pivotal trials that adequately demonstrate that our prescription drug product candidates are safe and effective for the intended indications. Likewise, to gain approval to market an animal prescription drug for a particular species, we must provide the FDA with safety and efficacy data from pivotal trials that adequately demonstrate that our prescription drug product candidates are safe and effective in the target species (e.g., dogs, cats or horses) for the intended indications. In addition, we must provide manufacturing data evidencing that we can produce our product candidates in accordance with cGMPs. For the FDA, we must also provide data from toxicology studies, also called target animal safety studies, and in some cases, environmental impact data. In addition to our

internal activities, we will partially rely on contract research organizations ("CROs") and other third parties to conduct our toxicology studies, biostatistical analysis, and certain other product development activities. The results of toxicology studies, other initial development activities, and/or any previous studies in humans or animals conducted by us or third parties may not be predictive of future results of pivotal trials or other future studies, and failure can occur at any time during the conduct of pivotal trials and other development activities by us or our CROs. Our pivotal trials may fail to show the desired safety or efficacy of our prescription drug product candidates despite promising initial data or the results in previous human or animal studies conducted by others. The success of a prescription drug product candidate in prior animal studies or in the treatment of humans does not ensure success in subsequent studies. Clinical trials in humans and pivotal trials in animals sometimes fail to show a benefit, even for drugs that are effective, because of statistical limitations in the design of the trials or other statistical anomalies. Therefore, even if our studies and other development activities are completed as planned, the results may not be sufficient to obtain the required regulatory approval for a product candidate.

Regulatory authorities can delay, limit, or deny approval of any of our prescription drug product candidates for many reasons, including:

- if they disagree with our interpretation of data from our pivotal studies or other development efforts;
- if we are unable to demonstrate to their satisfaction that our product candidate is safe and effective for the target indication and, if applicable, in the target species;
- if they require additional studies or change their approval policies or regulations;
- if they do not approve the formulation, labeling, or specifications of our current and future product candidates; and
- if they do not approve the manufacturing processes of our third-party contract manufacturers.

Further, even if we receive the required approval, such approval may be for a more limited indication than we originally requested, and the regulatory authority may not approve the labeling that we believe is necessary or desirable for successful commercialization.

Any delay or failure in obtaining any necessary regulatory approval for the intended indications of our human or animal product candidates would delay or prevent the commercialization of such product candidates and would harm our business and our operating results.

***The results of our earlier studies of Mytesi may not be predictive of the results in any future clinical trials and species-specific formulation studies, respectively, and we may not be successful in our efforts to develop or commercialize line extensions of Mytesi.***

Our human and animal product pipeline includes a number of potential indications of Mytesi, our lead prescription product. The results of our studies and other development activities and of any previous studies in humans or animals conducted by us or third parties may not be predictive of future results of these clinical studies and formulation studies, respectively. Failure can occur at any time during the conduct of these trials and other development activities. Even if our formulation/clinical studies and other development activities are completed as planned, the results may not be sufficient to pursue a particular line extension for Mytesi. Further, even if we obtain promising results from our clinical trials or species-specific formulation studies, as applicable, we may not successfully commercialize any line extension. Because line extensions are developed for a particular market, we may not be able to leverage our experience from the commercial launch of Mytesi in new markets. If we are not successful in developing and successfully commercializing these line extension products, we may not be able to grow our revenue, and our business may be harmed.

***Development of prescription drug products is inherently expensive, time-consuming and uncertain, and any delay or discontinuance of our current or future pivotal trials would harm our business and prospects.***

Development of prescription drug products for human and animal gastrointestinal health remains an inherently lengthy, expensive, and uncertain process, and our development activities may not be successful. We do not know whether our current or planned pivotal trials for any of our product candidates will begin or conclude on time, and they may be delayed or discontinued for a variety of reasons, including if we are unable to:

- address any safety concerns that arise during the course of the studies;
- complete the studies due to deviations from the study protocols or the occurrence of adverse events;
- add new study sites;
- address any conflicts with new or existing laws or regulations; or
- reach agreement on acceptable terms with study sites, which can be subject to extensive negotiation and may vary significantly among different sites.

Further, we may not be successful in developing new indications for Mytesi and Canalevia-CA1, and Neonorm may be subject to the same regulatory regime as prescription drug products in jurisdictions outside the US. Any delays in completing our development efforts will increase our costs, delay our development efforts and approval process, and jeopardize our ability to commence product sales and generate revenue. Any of these occurrences may harm our business, financial condition, and prospects. In addition, factors that may cause a delay in the commencement or completion of our development efforts may also ultimately lead to the denial of regulatory approval of our product candidates, which, as described above, would harm our business and prospects.

***We will partially rely on third parties to conduct our development activities. If these third parties do not successfully carry out their contractual duties, we may be unable to obtain regulatory approvals or commercialize our current or future human or animal product candidates on a timely basis or at all.***

We will partially rely upon Biostatisticians to conduct our toxicology studies and for other development activities. We intend to rely on CROs to conduct one or more of our planned pivotal trials. These CROs are not our employees, and except for contractual duties and obligations, we have limited ability to control the amount or timing of resources that they devote to our programs or manage the risks associated with their activities on our behalf. We are responsible for ensuring that each of our studies is conducted in accordance with the development plans and trial protocols presented to regulatory authorities. Any deviations by our CROs may adversely affect our ability to obtain regulatory approvals, subject us to penalties, or harm our credibility with regulators. The FDA and foreign regulatory authorities also require us and our CROs to comply with regulations and standards, GCPs or GLPs, for conducting, monitoring, recording, and reporting the results of our studies to ensure that the data and results are scientifically valid and accurate.

Agreements with CROs generally allow the CROs to terminate in certain circumstances with little or no advance notice. These agreements generally will require our CROs to reasonably cooperate with us at our expense for an orderly winding down of the CROs' services under the agreements. If the CROs conducting our studies do not comply with their contractual duties or obligations, if they experience work stoppages, do not meet expected deadlines, or if the quality or accuracy of the data they obtain is compromised, we may need to secure new arrangements with alternative CROs, which could be difficult and costly. In such an event, our studies may also need to be extended, delayed, or terminated as a result, or may need to be repeated. If any of the foregoing were to occur, regulatory approval, if required, and commercialization of our product candidates may be delayed, and we may be required to expend substantial additional resources.

***Even if we obtain regulatory approval for planned follow-on indications of crofelemer, Canalevia, or our other product candidates, they may never achieve market acceptance. Further, even if we are successful in the ongoing commercialization of Mytesi and Canalevia, we may not achieve commercial success.***

If we obtain necessary regulatory approvals for planned follow-on indications of crofelemer or our other product candidates, such products may still not achieve market acceptance and may not be commercially successful. Market acceptance of Mytesi, Canalevia, and any of our other products depends on a number of factors, including:

- the safety of our products as demonstrated in our target animal studies;
- the indications for which our products are approved or marketed;
- the potential and perceived advantages over alternative treatments or products, including generic medicines and competing products currently prescribed by physicians or veterinarians, as applicable, and, in the case of animal products, products approved for use in humans that are used extra-label in animals;
- the acceptance by physicians, veterinarians, and companion animal owners, as applicable, of our products as safe and effective;
- the cost in relation to alternative treatments and willingness on the part of physicians, veterinarians, patients, and animal owners, as applicable, to pay for our products;
- the prevalence and severity of any adverse side effects of our products;
- the relative convenience and ease of administration of our products; and
- the effectiveness of our sales, marketing, and distribution efforts.

Any failure by Mytesi or Canalevia to achieve market acceptance or commercial success would harm our financial condition and the results of operations.

***Human and animal gastrointestinal health products are subject to unanticipated post-approval safety or efficacy concerns, which may harm our business and reputation.***

The success of our commercialization efforts will depend upon the perceived safety and effectiveness of human and animal gastrointestinal health products, in general, and of our products, in particular. Unanticipated safety or efficacy concerns can subsequently arise with respect to approved prescription drugs products, such as Mytesi, or non-prescription products, such as Neonorm, which may result in product recalls or withdrawals or suspension of sales, as well as product liability and other claims. Any safety or efficacy concerns, recalls, withdrawals, or suspensions of sales of our products could harm our reputation and business, regardless of whether such concerns or actions are justified.

***Future federal and state legislation may result in increased exposure to product liability claims, which could result in substantial losses.***

Under current federal and state laws, companion and production animals are generally considered to be the personal property of their owners and as such, the owners' recovery for product liability claims involving their companion and production animals may be limited to the replacement value of the animal. Companion animal owners and their advocates, however, have filed lawsuits from time to time seeking non-economic damages such as pain and suffering and emotional distress for harm to their companion animals based on theories applicable to personal injuries to humans. If new legislation is passed to allow recovery for such non-economic damages, or if precedents are set allowing for such recovery, we could be exposed to increased product liability claims that could result in substantial

losses to us if successful. In addition, some horses can be worth millions of dollars or more, and product liability for horses may be very high. While we currently have product liability insurance, such insurance may not be sufficient to cover any future product liability claims against us.

***If we fail to retain current members of our senior management or to identify, attract, integrate, and retain additional key personnel, our business will be harmed.***

Our success depends on our continued ability to attract, retain, and motivate highly qualified management and scientific personnel. We are highly dependent upon our senior management, particularly Lisa A. Conte, our president and Chief Executive Officer. The loss of services of any of our key personnel would cause a disruption in our ability to develop our current or future product pipeline and commercialize our products and product candidates. Although we have offer letters with these key members of senior management, such agreements do not prohibit them from resigning at any time. To help attract, retain, and motivate qualified management and other personnel, we use share-based incentive awards such as employee stock options and restricted stock units. However, given the volatility in our stock price, it may be more difficult and expensive to recruit and retain employees, particularly senior management, through grants of stock or stock options. If our share-based compensation ceases to be viewed as a valuable benefit, our ability to attract, retain, and motivate qualified management and other personnel could be weakened, which could harm our results of operations and adversely affect the timing or outcomes of our current and planned studies, as well as the prospects for commercializing our products.

In addition, competition for qualified personnel in the human gastrointestinal health field is intense because there are a limited number of individuals who are trained or experienced in the field. We will need to hire additional personnel as we expand our product development and commercialization activities. Even if we are successful in hiring qualified individuals, as we are a growing organization, we do not have a track record for integrating and retaining individuals. If we are not successful in identifying, attracting, integrating or retaining qualified personnel on acceptable terms, or at all, our business will be harmed.

***We are dependent on two suppliers for the raw materials used to produce the active pharmaceutical ingredients in Mytesi and Canalevia. The termination of either of these contracts would result in a disruption to product development and harm our business.***

The raw material used to manufacture Mytesi and Canalevia-CA1 is CPL derived from the *Croton lechleri* tree, which is found in countries in South America, principally Peru. The ability of our contract suppliers to harvest CPL is governed by the terms of their respective agreements with local government authorities. Although CPL is available from multiple suppliers, we only have contracts with two suppliers to obtain CPL and arrange the shipment to our contract manufacturer. Accordingly, if our contract suppliers do not or are unable to comply with the terms of our respective agreements, and we are not able to negotiate new agreements with alternate suppliers on terms that we deem commercially reasonable, it may harm our business and prospects. The countries from which we obtain CPL could change their laws and regulations regarding the export of natural products or impose or increase taxes or duties payable by exporters of such products. Restrictions could be imposed on the harvesting of the natural products, or additional requirements could be implemented for the replanting and regeneration of the raw material. Such events could have a significant impact on our cost and ability to produce Mytesi, Canalevia-CA1, and anticipated line extensions.

***We are dependent upon third-party contract manufacturers, both for the supply of the active pharmaceutical ingredient in Mytesi and Canalevia-CA1, as well as for the supply of finished products for commercialization.***

We are in negotiations with Indena for the purification of the CPL received from our suppliers into the API used to manufacture Canalevia-CA1 and Mytesi, as well as the botanical extract in Neonorm. Indena has never manufactured either such ingredient on a commercial scale. Glenmark is the current manufacturer of crofelemer, the active API in Canalevia-CA1 and Mytesi. As announced in October 2015, we have entered into an agreement with Patheon, a provider of drug development and delivery solutions, under which Patheon provides enteric-coated tablets to us for use in humans and animals. We also may contract with additional third parties for the formulation and supply of finished products, which we will use in our planned studies and commercialization efforts.

We are dependent upon our contract manufacturers for the supply of the API in Mytesi and Canalevia-CA1. We currently have sufficient quantities of the API used in Mytesi and Canalevia to support our projected sales efforts. We are working with our contract manufacturers to increase the API manufacturing capacity of the API to support the sales forecast for 2024 and beyond. If our contract manufacturer cannot manufacture sufficient quantities of the API in a timely manner, we could suffer losses due to lost sales opportunities. We currently have sufficient quantities of the botanical extract used in Neonorm and Equilevia to support planned commercialization efforts for Neonorm and Equilevia. If we are not successful in reaching agreements with third parties on terms that we consider commercially reasonable for manufacturing and formulation of Mytesi and Canalevia-CA1, or if our contract manufacturer and formulator are not able to produce sufficient quantities or quality of the Mytesi and Canalevia-CA1 API or finished product under their agreements, it could delay our plans and harm our business prospects. For example, as a result of the outbreak in 2020 of SARS-CoV-2, the virus that causes COVID-19, which originated in Wuhan, China, and then spread globally, our suppliers and contract manufacturers could be disrupted by worker absenteeism, quarantines, or other travel or health-related restrictions or could incur increased costs associated with ensuring the safety and health of their personnel. If our suppliers or contract manufacturers are so affected, our supply chain could be disrupted, our product shipments could be delayed, our costs could be increased, and our business could be adversely affected.

The facilities used by our third-party contractors are subject to inspections, including by the FDA and other regulators, as applicable. We also depend on our third-party contractors to comply with cGMPs. If our third-party contractors do not maintain compliance with these strict regulatory requirements, they and we will not be able to secure or maintain regulatory approval for their facilities, which would have an adverse effect on our operations. In addition, in some cases, we also depend on our third-party contractors to produce supplies in conformity with our specifications, maintain quality control and quality assurance practices, and not employ disqualified personnel. If the FDA or a comparable foreign regulatory authority does not approve the facilities of our third-party contractors if so required, or if it withdraws any such approval in the future, we may need to find alternative manufacturing or formulation facilities, which could result in delays in our ability to develop or commercialize our products, if at all. We and our third-party contractors also may be subject to penalties and sanctions from the FDA and other regulatory authorities for any violations of applicable regulatory requirements. The EMA employs different regulatory standards than the FDA, so we may require multiple manufacturing processes and facilities for the same product candidate or any approved product. We are also exposed to risk if our third-party contractors do not comply with the negotiated terms of our agreements or if they suffer damage or destruction to their facilities or equipment.

***If we are unable to establish sales capabilities on our own or through third parties, we may not be able to market and sell our current or future human products and product candidates, if approved, and generate product or other revenue.***

We currently have limited sales, marketing, or distribution capabilities, and prior to Napo's launch of Mytesi for the symptomatic relief of noninfectious diarrhea in adults with HIV/AIDS on antiretroviral therapy, and our launch of Neonorm for pre-weaned dairy calves and Canalevia for CID in dogs, we had no experience in the sale, marketing, and distribution of human or animal health products. There are significant risks involved in building and managing a sales organization, including our potential inability to attract, hire, retain, and motivate qualified individuals, generate sufficient sales leads, provide adequate training to sales and marketing personnel, and effectively oversee a geographically dispersed sales and marketing team. Any failure or delay in the development of our internal sales, marketing, and distribution capabilities and entry into adequate arrangements with distributors or other partners would adversely impact the commercialization of Mytesi and Canalevia-CA1. If we are not successful in commercializing Mytesi and/or Canalevia-CA1, for their respective currently approved or conditionally approved indications or for any potential follow-on indications, either on our own or through one or more distributors, or in generating upfront licensing or other fees, including through the previously announced licensing arrangement between Napo Pharmaceuticals, Inc. and Napo Therapeutics S.p.A., we may never generate significant revenue and may continue to incur significant losses, which would harm our financial condition and results of operations.

***We will need to increase the size of our organization and may not successfully manage such growth.***

As of December 31, 2023, we had forty-nine employees. Our ability to manage our growth effectively will require us to hire, train, retain, manage, and motivate additional employees and to implement and improve our operational, financial, and management systems. These demands also may require the hiring of additional senior management personnel or the development of additional expertise by our senior management personnel. If we fail to expand and enhance our operational, financial, and management systems in conjunction with our potential future growth, it could harm our business and operating results.

***Canalevia-CA1 and our animal health prescription drug product candidates, if approved, may be marketed in the US only in the target animals and for the indications for which they are approved, and if we want to expand the approved animals or indications, it will need to obtain additional approvals, which may not be granted.***

We may market or advertise Canalevia-CA1 and our animal health prescription drug product candidates approved by regulatory authorities only in the specific species and for treatment of the specific indications for which they were approved, which could limit the use of the products by veterinarians and animal owners. We intend to develop, promote, and commercialize approved products for new animal treatment indications in the future, but we cannot be certain whether or at what additional time and expense we will be able to do so. If we do not obtain marketing approvals for new indications, our ability to expand our animal health business may be harmed.

Under the Animal Medicinal Drug Use Clarification Act of 1994, veterinarians are permitted to prescribe extra-label uses of fully approved animal drugs and approved human drugs for animals under certain conditions. While veterinarians may in the future prescribe and use human-approved products or use our products for extra-label uses, we may not promote our animal health products for extra-label uses. We note that extra-label uses are uses for which the product has not received approval. If the FDA determines that any of our marketing activities constitute promotion of an extra-label use, we could be subject to regulatory enforcement, including seizure of any misbranded or mislabeled drugs, and civil or criminal penalties, any of which could have an adverse impact on our reputation and expose us to potential liability. We will continue to spend resources ensuring that our promotional claims for our animal health products and product candidates remain compliant with applicable FDA laws and regulations, including materials we post or link to on our website. For example, in 2012, our Chief Executive Officer received an "untitled letter" from the FDA while at Napo regarding pre-approval promotion statements constituting misbranding of crofelemer, which was then an investigational drug. These statements were included in archived press releases included on Napo's website. Napo was required to expend time and resources to revise its website to remove the links in order to address the concerns raised in the FDA's letter.

***The misuse or extra-label use of Mytesi, Canalevia and our human or animal prescription drug product candidates approved by regulatory authorities may harm our reputation or result in financial or other damages.***

If our human or animal prescription drug product candidates are approved by regulatory authorities, there may be increased risk of product liability if physicians, veterinarians, patients, animal owners or others, as applicable, attempt to use such products extra-label, including the use of our products for indications or in species for which they have not been approved. Furthermore, the use of an approved human or animal drug such as Mytesi and Canalevia for indications other than those indications for which such products have been approved may not be effective, which could harm our reputation and lead to an increased risk of litigation. If we are deemed by a governmental or regulatory agency to have engaged in the promotion of any approved human or animal product for extra-label use, such agency could request that we modify our training or promotional materials and practices, and we could be subject to significant fines and penalties, and the imposition of these sanctions could also affect our reputation and position within the gastrointestinal health industry. Any of these events could harm our reputation and our operating results.

***We may be unable to obtain, or obtain on a timely basis, a renewal of conditional approval for Canalevia-CA1 or to eventually obtain full regulatory approval of Canalevia-CA1, which would harm our operating results.***

On December 21, 2021, the FDA conditionally approved Canalevia-CA1 (crofelemer delayed-release tablets) for the treatment of CID in dogs under application number 141-552. FDA's conditional approval allows the Company

to legally sell Canalevia-CA1 before proving it meets the "substantial evidence" standard of effectiveness for full approval. The Company may request renewal of the conditional approval annually for up to four more years, for a total of five years of conditional approval. To receive a renewal from FDA, the Company must show active progress toward proving "substantial evidence of effectiveness" for full approval.

If the FDA grants all four annual renewals, the Company has up to four-and-a-half years to develop and submit the necessary data to complete the effectiveness requirement. If the Company does not submit all necessary information to support full approval of Canalevia-CA1 by this four-and-a-half-year deadline, the conditional approval terminates immediately. The Company would then be required to stop marketing the drug because it would be considered to be unapproved.

If the Company submits the necessary information before the four-and-a-half-year deadline, the conditional approval period runs another six months, for a total of five years, while the FDA reviews the application for full approval. The conditional approval automatically terminates five years after the date of the initial conditional approval. If FDA does not fully approve the drug before the five-year termination date, the Company would then have to stop marketing the drug because it would be considered to be unapproved.

***We may not maintain the benefits associated with MUMS designation, including market exclusivity.***

Although we have received MUMS designation for Canalevia-CA1 for the treatment of CID in dogs, we may not maintain the benefits associated with MUMS designation. MUMS designation is a status similar to "orphan drug" status for human drugs. When we were granted MUMS designation for Canalevia-CA1 for the indication of CID in dogs, we became eligible for incentives to support the approval or conditional approval of the designated use. This designation does not allow us to commercialize a product until such time as we obtain approval or conditional approval of the product.

Because Canalevia-CA1 has received MUMS designation for the identified particular intended use, we are eligible to obtain seven years of exclusive marketing rights upon approval (or conditional approval) of Canalevia-CA1 for that intended use and become eligible for grants to defray the cost of our clinical work. Each designation that is granted must be unique, i.e., only one designation can be granted for a particular API in a particular dosage form for a particular intended use. The intended use includes both the target species and the disease or condition to be treated.

At some point, we could lose MUMS designation. The basis for a lost designation can include but is not limited to, our failure to engage with due diligence in moving forward with a non-conditional approval. In addition, MUMS designation may be withdrawn for a variety of reasons such as where the FDA determines that the request for designation was materially defective, or if the manufacturer is unable to assure sufficient quantity of the prescription drug product to meet the needs of animals with the rare disease or condition. If this designation is lost, it could have a negative impact on the product and us, which includes but is not limited to, market exclusivity related to MUMS designation, or eligibility for grants as a result of MUMS designation.

***The market for our human and animal products, and the gastrointestinal health market as a whole, is uncertain and may be smaller than we anticipate, which could lead to lower revenue and harm our operating results.***

It is very difficult to estimate the commercial potential of any of our human or animal products because the gastrointestinal health market continues to evolve and it is difficult to predict the market potential for our products. The market will depend on important factors such as safety and efficacy compared to other available treatments, changing standards of care, preferences of physicians, as applicable, the willingness of patients, as applicable, to pay for such products, and the availability of competitive alternatives that may emerge either during the product development process or after commercial introduction. If the market potential for our human or animal products is less than we anticipate due to one or more of these factors, it could negatively impact our business, financial condition and results of operations. Further, the willingness of patients to pay for our products may be less than we anticipate, and may be negatively affected by overall economic conditions.

***Insurance coverage for Mytesi for its current approved indication could decrease or end, or Mytesi might not receive insurance coverage for any approved follow-on indications, which could lead to lower revenue and harm our operating results.***

For its current approved indication, Mytesi is currently reimbursed by almost all of commercial and Medicare insurance plans. Mytesi is currently covered by Medicaid in all 50 states. However, the nature or extent of coverage for Mytesi by any of these plans or programs could change or be terminated, or Mytesi might not receive insurance coverage for any approved follow-on indications. Either outcome could lead to significantly lower revenue and significantly harm our operating results.

***We may engage in future acquisitions that increase our capital requirements, dilute our stockholders, cause us to incur debt or assume contingent liabilities and subject us to other risks.***

We may evaluate various strategic transactions, including licensing or acquiring complementary products, technologies, or businesses. Any potential acquisitions may entail numerous risks, including increased operating expenses and cash requirements, assimilation of operations and products, retention of key employees, diversion of our management's attention, and uncertainties in our ability to maintain key business relationships of the acquired entities. In addition, if we undertake acquisitions, we may issue dilutive securities, assume or incur debt obligations, incur large one-time expenses, and acquire intangible assets that could result in significant future amortization expenses. Moreover, we may not be able to locate suitable acquisition opportunities, and this inability could impair our ability to grow or obtain access to technology or products that may be important to the development of our business.

***Certain of the countries in which we plan to commercialize our products in the future are developing countries, some of which have potentially unstable political and economic climates.***

We may commercialize our products in jurisdictions that are developing and emerging countries. This may expose us to the impact of political or economic upheaval, and we could be subject to unforeseen administrative or fiscal burdens. At present, we are not insured against the political and economic risks of operating in these countries. Any significant changes to the political or economic climate in any of the developing countries in which we operate or plan to sell products either now or in the future may substantially affect our business, financial condition, trading performance, and prospects.

***Fluctuations in the exchange rate of foreign currencies could result in currency transaction losses.***

As we expand our operations, we expect to be exposed to risks associated with foreign currency exchange rates. We anticipate that we may commercialize Mytesi and Canalevia-CA1 and its line extensions in jurisdictions outside the US. As a result, we may also be further affected by fluctuations in exchange rates in the future to the extent that sales are denominated in currencies other than US dollars. We do not currently employ any hedging or other strategies to minimize this risk, although we may seek to do so in the future.

***Laws and regulations governing global trade compliance could adversely impact our business.***

The US Department of the Treasury's Office of Foreign Assets Control ("OFAC") and the Bureau of Industry and Security ("BIS") at the US Department of Commerce administer certain laws and regulations that restrict US persons and, in some instances, non-US persons, in conducting activities, transacting business with or making investments in certain countries, governments, entities and individuals subject to US economic sanctions. In addition, engaging in sales activities to foreign governments introduces additional compliance risks, including risks specific to anti-bribery regulations, including the US Foreign Corrupt Practices Act of 1977, as amended, or the FCPA, the U.K. Bribery Act 2010 and other similar statutory requirements prohibiting bribery and corruption in the jurisdictions in which we operate. The FCPA prohibits US corporations and their representatives from offering, promising, authorizing, or making payments to any foreign government official, government staff member, political party, or political candidate in an attempt to obtain or retain business abroad. The scope of the FCPA includes interactions with certain healthcare professionals in many countries. Other countries have enacted similar anti-corruption laws and/or regulations.

Our international operations subject us to these laws and regulations, which are complex, restrict our business dealings with certain countries, governments, entities, and individuals, and are constantly changing. Further restrictions may be enacted, amended, enforced, or interpreted in a manner that materially impacts our operations.

Violations of these regulations are punishable by civil penalties, including fines, denial of export privileges, injunctions, asset seizures, debarment from government contracts, and revocations or restrictions of licenses, as well as criminal fines and imprisonment. We have established policies and procedures designed to assist with our compliance with such laws and regulations. However, there can be no assurance that our policies and procedures will prevent us from violating these regulations in every transaction in which we may engage or that any businesses that we may acquire have complied with such regulations, and such a violation could adversely affect our reputation, business, financial condition, results of operations and cash flows.

***There are other gastrointestinal-focused human pharmaceutical companies, and we face competition in the marketplaces in which we operate or plan to operate.***

Our commercial success in the human drug arena remains dependent on maintaining or establishing a competitive position in the market for the currently approved specialty indication of Mytesi as well as for planned Mytesi follow-on indications. In the IBS-D market, in particular, several competitors have commercially available products approved for our planned IBS-D indication. The availability of our competitors' products could limit the demand and the price we are able to charge for any drug candidate we develop. The inability to compete with existing or subsequently introduced drug candidates would have a material adverse impact on our business, financial condition, and prospects.

***Our obligations to Streeterville are secured by a security interest in all of Napo's NP-300 assets, so if we default on those obligations, Streeterville could foreclose on our assets.***

Our obligations under the secured promissory note issued to Streeterville Capital, LLC ("Streeterville") are secured by a first priority security interest in all existing and future NP-300 technology held by Napo, including intellectual property, as provided in the Security Agreement, dated January 19, 2021, between Napo and Streeterville. As a result, if we default on our obligations under these agreements, Streeterville could foreclose on its security interests and liquidate some or all of these assets, which would harm our plans to develop and commercialize NP-300, financial condition and results of operations and could require us to reduce or cease operations with respect to NP-300.

***Our royalty interests require us to make minimum royalty payments, even if we do not sell a sufficient amount of products to cover such payments, which may strain our cash resources.***

Since March 2020, we have sold royalty interests to certain lenders that entitle such lenders to receive future royalties on sales of our products. These royalty interests require us to make minimum royalty payments beginning in 2021, even if we do not sell a sufficient amount of product to cover such payments, which may strain our cash resources. The total minimum royalty payments will be approximately \$14.6 million in 2024, \$19.5 million in 2025, and \$5.3 million in 2026.

***Failure in our information technology systems, including cyber-attacks or other data security incidents, could significantly disrupt our operations.***

Our operations depend, in part, on the continued performance of our information technology systems. Our information technology systems are potentially vulnerable to physical or electronic break-ins, computer viruses, phishing attacks, and other types of disruptions. We have and continue to experience cyber-attacks of varying degrees. Our security measures may also be breached due to employee error, malfeasance, system errors or other vulnerabilities. Such breach or unauthorized access or attempts by outside parties to fraudulently induce employees or users to disclose sensitive information in order to gain access to our data could result in significant legal and financial exposure, and damage to our reputation that could potentially have an adverse effect on our business. Because the

techniques used to obtain unauthorized access or sabotage systems change frequently, become more sophisticated, and often are not recognized until launched against a target, we may be unable to anticipate these techniques or implement adequate preventative measures. Additionally, cyber-attacks could also compromise trade secrets and other sensitive information and result in such information being disclosed to others and becoming less valuable, which could negatively affect our business. Although we have information technology security systems, a successful cybersecurity attack or other data security incident could result in the misappropriation and/or loss of confidential or personal information, create system interruptions, deploy malicious software that attacks our systems, or result in financial losses. It is possible that a cybersecurity attack might not be noticed for some period of time. The occurrence of a cyber-security attack or incident could result in business interruptions from the disruption of our information technology systems or negative publicity resulting in reputational damage to our stockholders and other stakeholders and/or increased costs to prevent, respond to, or mitigate cybersecurity events. In addition, the unauthorized dissemination of sensitive personal information or proprietary or confidential information could expose us or other third parties to regulatory fines or penalties, litigation, and potential liability, or otherwise harm our business.

***Global macroeconomic conditions may negatively affect us and may magnify certain risks that affect our business.***

Our business is sensitive to general economic conditions, both inside and outside the US Slower global economic growth, credit market crises, high levels of unemployment, reduced levels of capital expenditures, government deficit reduction, changes in inflation and interest rate environments, sequestration and other austerity measures and other challenges affecting the global economy adversely affects us and our distributors, customers, and suppliers. It is uncertain how long these effects will last or whether economic and financial trends will worsen or improve. Changes in economic conditions, supply chain constraints, and steps taken by governments and central banks could lead to higher inflation than previously experienced or expected, which could, in turn, lead to an increase in costs. In an inflationary environment, we may be unable to raise the prices of our products sufficiently to keep up with the rate of inflation. Such uncertain economic times may have a material adverse effect on our revenues, results of operations, financial condition, and, if circumstances worsen, our ability to raise capital at reasonable rates. If slower growth in the global economy or in any of the markets we serve continues for a significant period, if there is significant deterioration in the global economy or such markets, or if improvements in the global economy don't benefit the markets we serve, our business and financial statements could be adversely affected.

Additionally, as a result of any future global economic downturn, our third-party payers may delay or be unable to satisfy their reimbursement obligations. Sales of our principal products are dependent, in part, on the availability and extent of reimbursement from third-party payers, including government programs such as Medicare and Medicaid and private-payer healthcare and insurance programs. A reduction in the availability or extent of reimbursement from government and/or private payer healthcare programs could have a material adverse effect on the sales of our products, our business, and the results of our operations.

Current economic conditions may adversely affect the ability of our distributors, customers, suppliers, and service providers to obtain the liquidity required to pay for our products or to buy necessary inventory or raw materials and to perform their obligations under agreements with us, which could disrupt our operations, and could negatively impact our business and cash flow. Although we make efforts to monitor these third parties' financial condition and their liquidity, our ability to do so is limited, and some of them may become unable to pay their bills in a timely manner or may even become insolvent, which could negatively impact our business and results of operations. These risks may be elevated with respect to our interactions with third parties with substantial operations in countries where current economic conditions are the most severe, particularly where such third parties are themselves exposed to sovereign risk from business interactions directly with fiscally challenged government payers.

At the same time, significant changes and volatility in the financial markets, in the consumer and business environment, in the competitive landscape, and in the global political and security landscape make it increasingly difficult for us to predict our revenues and earnings into the future. As a result, any revenue or earnings guidance or outlook that we have given or might give may be overtaken by events or may otherwise turn out to be inaccurate. Though we endeavor to give reasonable estimates of future revenues and earnings at the time we give such guidance, based on then-current conditions, there is a significant risk that such guidance or outlook will turn out to be, or to have been, incorrect.

***Unfavorable global economic conditions could adversely affect our business, financial condition, or results of operations.***

Our business, financial condition, results of operations, or prospects could be adversely affected by general conditions in the global economy and in the global financial markets. A severe or prolonged economic downturn, including as a result of the COVID-19 pandemic, the ongoing war in Ukraine, interest rate fluctuations, rising inflation, recession, or other global financial or geopolitical crises, could result in a variety of risks to our business, including weakened demand for our product candidates, if approved, or our ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy could also strain our suppliers and contract manufacturing organizations ("CMO"), possibly resulting in supply or manufacturing disruption. Any of the foregoing could harm our business and we cannot anticipate all the ways in which such conditions could adversely impact our business.

***Substantially all of our revenue for recent periods has been received from two customers.***

Substantially all of our revenue has been derived from two customers. Except for the shelter-in-place mandate, we have not been made aware by our customers if they have experienced other issues arising due to COVID-19 that may materially impact our financial condition, liquidity or results of operations. We will continue to have dialogues with our customers.

***The Company's ability to attract and retain qualified members of our board of directors may be impacted due to new state laws, including recently enacted gender quotas.***

In September 2018, California enacted SB 826 requiring public companies headquartered in California to maintain minimum female representation on their boards of directors as follows: requiring public companies headquartered in California to maintain minimum female representation on their boards of directors as follows: by December 31, 2019, public company boards must have a minimum of one female director; by December 31, 2021, public company boards with five members must have at least two female directors, and public company boards with six or more members will be required to have at least three female directors.

Additionally, on September 30, 2020, California enacted AB 979, requiring public companies with principal executive offices in California to each have at least one director from an underrepresented community based on ethnicity and sexual orientation by December 31, 2021. By December 31, 2022, each of these companies must have at least two directors from such underrepresented communities if such company has more than four but fewer than nine directors or at least three directors from underrepresented communities if the company has nine or more directors.

Each of these measures has been challenged in court, and although judges of the California Superior Court ruled that AB 979 and SB 826 violate the California constitution in April 2022 and May 2022, respectively, the Secretary of State of the State of California has appealed such rulings, and the ultimate enforceability of these or similar laws remains uncertain.

In addition, the Company is subject to the listing rules from Nasdaq related to board diversity and disclosure, which require all companies listed on Nasdaq's US exchanges to disclose consistent, transparent diversity statistics regarding their board of directors publicly. Additionally, the rules require most Nasdaq-listed companies to have, or explain why they do not have, at least two diverse directors, including one who self-identifies as female and one who self-identifies as either an underrepresented minority or LGBTQ+.

Failure to achieve designated minimum gender and diversity levels in a timely manner exposes such companies to financial penalties and reputational harm. While we are currently in compliance with these regulations, we cannot assure that we can recruit, attract and/or retain qualified members of the board and meet gender and diversity quotas as a result of the California laws or Nasdaq rules, which may expose us to penalties and/or reputational harm.

***Evolving expectations around corporate responsibility practices, specifically related to ESG matters, may expose us to reputational and other risks.***

Investors, stockholders, customers, suppliers, and other third parties are increasingly focusing on ESG and corporate social responsibility endeavors and reporting. Companies that do not adapt to or comply with the evolving investor or stakeholder expectations and standards or which are perceived to have not responded appropriately may suffer from reputational damage and result in the business, financial condition and/or stock price of a company being materially and adversely affected. Further, this increased focus on ESG issues may result in new regulations and/or third-party requirements that could adversely impact our business or certain stockholders reducing or eliminating their holdings of our stock. Additionally, an allegation or perception that we have not taken sufficient action in these areas could negatively harm our reputation.

***The growing use of AI systems to automate processes, analyze data, and support decision-making poses inherent risks.***

Flaws, biases, or malfunctions in systems powered by AI could lead to operational disruptions, data loss, or erroneous decision-making, that may impact business operations, financial condition, and reputation. Ethical and legal challenges may arise, including biases or discrimination in AI outcomes, non-compliance with data protection regulations, and lack of transparency. Furthermore, the deployment of AI systems could expose the Company to increased cybersecurity threats, such as data breaches and unauthorized access leading to financial losses, legal liabilities, and reputational damage. The Company also faces competitive risks if it fails to adopt AI or other machine learning technologies in a timely fashion.

**Risks Related to Intellectual Property**

***We cannot be certain that our patent strategy will be effective in protecting against competition.***

Our commercial success depends in large part on obtaining and maintaining patent, trademark, and trade secret protection of our human or animal products, both prescription and non-prescription, our current human or animal product candidates and any future human or animal product candidates, and their respective components, formulations, methods used to manufacture them and methods of treatment, as well as successfully defending our patents and other intellectual property rights against third-party challenges. Our ability to stop unauthorized third parties from making, using, selling, offering to sell, or importing our products or our product candidates is dependent upon the extent to which we have rights under valid and enforceable patents, trade secrets, and other similar intellectual property that cover these activities. The patent prosecution process is expensive and time-consuming, and we may not be able to prepare, file, and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of inventions made in the course of development and commercialization activities in time to obtain patent protection on them.

We have a portfolio of US and foreign-issued patents and pending applications related to our products and product candidates. We have issued three US patents, which are listed in the FDA's Orange Book for Mytesi. We plan to rely on certain of these issued patents as protection for Canalevia. The strength of patents in the field of pharmaceuticals and animal health involves complex legal and scientific questions and can be uncertain. We cannot be certain that pending applications will be issued as patents. For those patents that are already issued and even if other patents are successfully issued, third parties may challenge their validity, enforceability, or scope, which may result in such patents being narrowed, invalidated, or held unenforceable. Furthermore, even if they are unchallenged, our patents may not adequately protect our intellectual property or prevent others from designing around their claims. If the patents we have are not maintained, their scope is significantly narrowed, or if we cannot obtain issued patents from pending applications, our business and prospects will be harmed.

The Leahy-Smith America Invents Act, patent reform legislation enacted in 2011, could increase the uncertainties and costs surrounding the prosecution of any patent applications and the enforcement or defense of any patents that are issued. The Leahy-Smith Act introduced significant changes to US patent law. These include provisions that affect the way patent applications are prosecuted, redefine prior art, may affect patent litigation, and

switch the US patent system from a “first-to-invent” system to a “first-to-file” system. Under a “first-to-file” system, assuming the other requirements for patentability are met, the first inventor to file a patent application is generally entitled to the patent on an invention regardless of whether another inventor had made the invention earlier. The USPTO developed regulations and procedures to govern the administration of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act, and in particular, the first-to-file provisions, became effective on March 16, 2013. Among some of the other changes to the patent laws are changes that limit where a patentee may file a patent infringement suit and that provide opportunities for third parties to challenge any issued patent in the USPTO. The Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our patents and any other patents that are issued, all of which could harm our business and financial condition.

***Obtaining and maintaining our patent protection depends on compliance with various procedural requirements, document submission, fee payment, and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.***

Periodic maintenance and annuity fees on any issued patent and, in certain jurisdictions, pending applications are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patent. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment, and other similar provisions during the patent application process. While an inadvertent lapse can, in many cases, be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include failure to respond to official actions within prescribed time limits, non-payment of fees, and failure to properly legalize and submit formal documents. If we fail to maintain the patents and patent applications covering our prescription drug products, prescription drug product candidates, and non-prescription products, our competitors might be able to enter the market, which would harm our business.

***Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, which would be costly and time-consuming and, if successfully asserted against us, delay or prevent the development and commercialization of our current or future products and product candidates.***

Our research, development, and commercialization activities may infringe, otherwise violate, or be claimed to infringe or otherwise violate patents owned or controlled by other parties. There may be patents already issued that we are unaware of that might be infringed by a product or one of our current or future prescription drug product candidates or non-prescription products. Moreover, it is also possible that patents may exist that we are aware of but that we do not believe are relevant to our current or future prescription drug product candidates or non-prescription products, which could nevertheless be found to block our freedom to market these products. Because patent applications can take many years to issue and may be confidential for 18 months or more after filing, there may be applications now pending of which we are unaware and which may later result in issued patents that may be infringed by our current or future prescription drug product candidates or non-prescription products. We cannot be certain that our products, current or future prescription drug product candidates or non-prescription products will not infringe these or other existing or future third-party patents. In addition, third parties may obtain patents in the future and claim that the use of our technologies infringes upon these patents.

To the extent we become subject to future third-party claims against us or our collaborators, we could incur substantial expenses, and if any such claims are successful, we could be liable to pay substantial damages, including treble damages and attorney's fees if we or our collaborators are found to be willfully infringing a third-party's patents. If a patent infringement suit were brought against us or our collaborators, we or they could be forced to stop or delay research, development, manufacturing, or sales of the human or animal prescription drug or non-prescription product that is the subject of the suit. Even if we are successful in defending such claims, infringement and other intellectual property claims can be expensive and time-consuming to litigate and divert management's attention from our business and operations. As a result of or in order to avoid potential patent infringement claims, we or our collaborators may be compelled to seek a license from a third party for which we would be required to pay license

fees, royalties, or both. Moreover, these licenses may not be available on acceptable terms or at all. Even if we or our collaborators were able to obtain such a license, the rights may be nonexclusive, which could allow our competitors access to the same intellectual property. Any of these events could harm our business and prospects.

***Our proprietary position depends upon the botanical guidance of our drug approval and patents that are formulation or method-of-use patents, which do not prevent a competitor from using the same human or animal drug for another use.***

Composition-of-matter patents on the API in prescription drug products are generally considered to be the strongest form of intellectual property protection because such patents provide protection without regard to any particular method of use, manufacture, or formulation of the API used. The composition-of-matter patents for crofelemer, the API in Mytesi and Canalevia-CA1 have expired, and the issued patents and applications relevant to our products and product candidates cover methods of use for crofelemer and the botanical extract in Neonorm and Equilevia.

Method-of-use patents protect the use of a product for the specified method, and formulation patents cover formulations of the API or botanical extract. These types of patents do not prevent a competitor from developing or marketing an identical product for an indication that is outside the scope of the patented method or from developing a different formulation that is outside the scope of the patented formulation. Moreover, with respect to method-of-use patents, even if competitors do not actively promote their product for our targeted indications or uses for which we may obtain patents, physicians may recommend that patients use our products extra-label, and veterinarians may recommend that animal owners use these products extra-label, or animal owners may do so themselves. Although extra-label use may infringe or contribute to the infringement of method-of-use patents, the practice is common, and such infringement is difficult to prevent or prosecute.

***We may be involved in lawsuits to protect or enforce our patents, which could be expensive, time-consuming, and unsuccessful, and third parties may challenge the validity or enforceability of our patents, and they may be successful.***

We intend to rely upon a combination of regulatory exclusivity periods, patents, trade secret protection, and confidentiality agreements to protect the intellectual property related to Mytesi, our current prescription drug product candidates, non-prescription products, and our development programs.

If the breadth or strength of protection provided by any patents, patent applications, or future patents we may own, license, or pursue with respect to any of our current or future product candidates or products is threatened, it could threaten our ability to commercialize any of our current or future human or animal product candidates or products. Further, if we encounter delays in our development efforts, the period of time during which we could market any of our current or future product candidates or products under any patent protection we obtain would be reduced.

Given the amount of time required for the development, testing, and regulatory review of new product candidates or products, patents protecting such candidates might expire before or shortly after such product candidates or products are commercialized. The United States Patent and Trademark Office ("USPTO") has issued a patent term extension certificate extending the term of US 7,341,744 by 1,075 days under 35 U.S.C 156. With respect to requests for patent term extensions, the applicable authorities, including the USPTO and the FDA, and any equivalent regulatory authority in other countries, may not agree with our assessment of whether such extensions are available and may refuse to grant extensions to patents, or may grant more limited extensions than requested. If this occurs, our competitors may take advantage of our investment in development and trials by referencing our clinical and preclinical data and launching their product earlier than might otherwise be the case.

Even where laws provide protection, or we are able to obtain patents, costly and time-consuming litigation may be necessary to enforce and determine the scope of our proprietary rights, and the outcome of such litigation would be uncertain. Moreover, any actions we may take to enforce our intellectual property against our competitors could provoke them to bring counterclaims against us, and some of our competitors have substantially greater intellectual property portfolios than we have. To counter infringement or unauthorized use of any patents we may

obtain, we may be required to file infringement claims, which can be expensive and time-consuming to litigate. In addition, if we or one of our future collaborators were to initiate legal proceedings against a third party to enforce a patent covering one of our products, current product candidates, or one of our future products, the defendant could counterclaim that the patent is invalid or unenforceable. In patent litigation in the US, defendant counterclaims alleging invalidity or unenforceability are commonplace, and challenges to the validity of patents in certain foreign jurisdictions are common as well. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, non-enablement, or lack of statutory subject matter. Grounds for an unenforceability assertion could be an allegation that someone connected with the prosecution of the patent withheld relevant material information from the USPTO or made a materially misleading statement during prosecution. Under the Hatch-Waxman Act, a competitor seeking to market a generic form of Mytesi before the expiration of any of the patents listed in the FDA's Orange Book for Mytesi could file an ANDA with a certification under 21 U.S.C. § 3559(j)(2) (A)(iv) that each of these patents (except for those which the ANDA filer states it will market only after its expiration) is either invalid, unenforceable or not infringed. We may assert the patents in Hatch-Waxman litigation against the party filing the ANDA to keep the competing product off of the market until the patents expire, but there is a risk that we will not succeed. The party filing the ANDA may also counterclaim in the litigation that our patents are not valid or unenforceable, and the court may find one or more claims of our patents invalid or unenforceable. If this occurs, a competing generic product could be marketed prior to the expiration of our patents listed in the Orange Book, which would harm our business.

Third parties may also raise similar validity claims before the USPTO in post-grant proceedings such as *ex parte* reexaminations, *inter partes* review, or post-grant review, or oppositions or similar proceedings outside the US, in parallel with litigation or even outside the context of litigation. The outcome following legal assertions of invalidity and unenforceability is unpredictable. If a defendant were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of any future patent protection on one or more of our products or our current or future product candidates. Such a loss of patent protection could harm our business. We cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution or other basis for a finding of invalidity. Litigation proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. In addition, public announcements of the results of hearings, motions, or other interim proceedings or developments could be made public. If securities analysts or investors perceive these results to be unsuccessful, it could have an adverse effect on the price of our common stock. Finally, we may not be able to prevent misappropriation of our trade secrets or confidential information, particularly in countries where the laws may not protect those rights as fully as in the US.

***If we are unable to prevent disclosure of our trade secrets or other confidential information to third parties, our competitive position may be impaired.***

We also rely on trade secret protection and confidentiality agreements to protect proprietary know-how that is not patentable or for which we have not filed patent applications, processes for which patents are difficult to enforce, and other elements of our product development processes that involve proprietary know-how, information or technology that is not covered by patents. Although we require all of our employees to assign their inventions to us and endeavor to execute confidentiality agreements with all of our employees, consultants, advisors, and any third parties who have access to our proprietary know-how, information, or technology, we cannot be certain that we have executed such agreements with all parties who may have helped to develop our intellectual property or had access to our proprietary information, or that our agreements will not be breached. We cannot guarantee that our trade secrets and other confidential, proprietary information will not be disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. If we are unable to prevent disclosure of our intellectual property to third parties, we may not be able to maintain a competitive advantage in our market, which would harm our business.

Any disclosure to or misappropriation of our confidential, proprietary information by third parties could enable competitors to quickly duplicate or surpass our technological achievements.

***Changes in US patent law could diminish the value of patents in general, thereby impairing our ability to protect our products.***

As is the case with other human or animal pharmaceutical product companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the human and animal health industries involves both technological and legal complexity. Therefore, obtaining and enforcing patents is costly, time-consuming, and inherently uncertain. In addition, the US has recently enacted and implemented wide-ranging patent reform legislation. The US Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the US Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce patents that we have or that we might obtain in the future.

***We may not be able to protect our intellectual property rights throughout the world, which could impair our business.***

Filing, prosecuting and defending patents on human and animal drug products, product candidates and non-prescription products throughout the world would be prohibitively expensive. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we may obtain patent protection, but where patent enforcement is not as strong as that in the US. These products may compete with our products in jurisdictions where we do not have any issued or licensed patents and any future patent claims or other intellectual property rights may not be effective or sufficient to prevent them from so competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents and other intellectual property protection, particularly those relating to animal health products, which could make it difficult for us to stop the infringement of our future patents, if any, or patents we have in licensed, or marketing of competing products in violation of our proprietary rights generally. Further, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws of the US. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the US and abroad. Proceedings to enforce our future patent rights, if any, in foreign jurisdictions could result in substantial cost and divert our efforts and attention from other aspects of our business.

***Our business could be harmed if we fail to obtain certain registered trademarks in the US or in other countries.***

Our registered and pending US trademarks include MYTESI®, JAGUAR HEALTH®, the Jaguar Health Logo®, NAPO®, Napo Logo®, Napo Therapeutics, CANALEVIA, CANALEVIA-CA1, CANALEVIA-CA2, EQUILEVIA, NEONORM®, JAGUAR ANIMAL HEALTH®, and the Jaguar Animal Health Logo®. We also own registered and pending applications for the CANALEVIA mark in a number of foreign countries. During trademark registration proceedings, we may receive rejections of our trademark applications. If so, we will have an opportunity to respond, but we may be unable to overcome such rejections. In addition, the USPTO and comparable agencies in many foreign jurisdictions may permit third parties to oppose pending trademark applications and to seek to cancel registered trademarks. If opposition or cancellation proceedings are filed against any of our trademark applications or any registered trademarks, our trademarks may not survive such proceedings. Moreover, any name we propose to use with our prescription drug product candidates in the US, including CANALEVIA and CANALEVIA-CA1, must be approved by the FDA, regardless of whether we have registered or applied to register as a trademark. The FDA typically conducts a review of proposed prescription drug product names, including an evaluation of potential for confusion with other product names. If the FDA objects to any of our proposed proprietary product names, we may be required to expend significant additional resources in an effort to identify a suitable substitute name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA.

***We may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of third parties.***

We have received confidential and proprietary information from third parties. In addition, we employ individuals who were previously employed at other biotechnology, pharmaceutical or animal health companies. We may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise improperly used or disclosed confidential information of these third parties or our employees' former employers. Litigation may be necessary to defend against any such claims. Even if we were successful in defending against any such claims, such litigation could result in substantial cost and be a distraction to our management and employees.

***Even if we receive any of the required regulatory approvals for our current or future prescription drug product candidates and non-prescription products, we will be subject to ongoing obligations and continued regulatory review, which may result in significant additional expenses and delays.***

If the FDA or any other regulatory body approves any of our current or future prescription drug product candidates, or if necessary, our non-prescription products, the manufacturing processes, clinical development, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion and recordkeeping for the product may be subject to extensive and ongoing regulatory requirements. These requirements could include but are not limited to, submissions of efficacy and safety and other post-marketing information and reports, establishment registration, and product listing, compliance with new rules promulgated under the FSMA, as well as continued compliance with cGMPs, GLPs, and GCPs for any studies that we conduct post-approval. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with our contract manufacturers or manufacturing processes, or failure to comply with regulatory requirements, are reportable events to the FDA and may result in, among other things:

- restrictions on the marketing or manufacturing of the product, withdrawal of the product from the market, revised labeling, or voluntary or involuntary product recalls;
- additional clinical studies, fines, warning letters or holds on target animal studies;
- refusal by the FDA, or other regulators to approve pending applications or supplements to approved applications filed by us or our strategic collaborators related to the unknown problems, or suspension or revocation of the problematic product's license approvals;
- product seizure or detention, or refusal to permit the import or export of products; and
- injunctions and/or the imposition of civil or criminal penalties.

The FDA or other regulatory agency's policies may change, and additional government regulations may be enacted that could prevent, limit, or delay regulatory approval of our product candidates or require certain changes to the labeling or additional clinical work concerning the safety and efficacy of the product candidates. We cannot predict the likelihood, nature, or extent of government regulation that may arise from future legislation or administrative action in the US or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, and we may not achieve or sustain profitability, which would harm our business. In addition, failure to comply with these regulatory requirements could result in significant penalties and delays.

In addition, from time to time, we may enter into consulting and other financial arrangements with physicians or veterinarians, who prescribe or recommend our products once approved. As a result, we may be subject to state, federal, and foreign healthcare and/or veterinary medicine laws. If our financial relationships with veterinarians are found to be in violation of such laws that apply to us, we may be subject to penalties.

Further, our commercial supply is regulated by the FDA, which requires regular filings of annual reports and may include modifications by the Company to our approvals. Failure to gain agreement from the FDA on a timely basis could adversely affect our commercial supply of products.

Lastly, if we obtain conditional approval for our current or future drug product candidates, this conditional approval is renewable annually for five years and may be withdrawn or terminated under certain circumstances either during or at the end of the five-year period. For example, even though we have obtained conditional approval for Canalevia-CA1, if we do not undertake substantial efforts to do additional clinical research each year for the next five years, the FDA could terminate such conditional approval by refusing to renew the conditional approval.

***Any of our current or future prescription drug product candidates or non-prescription products may cause or contribute to adverse medical events that we would be required to report to regulatory authorities and if we fail to do so, we could be subject to sanctions that would harm our business.***

If we are successful in commercializing any of our current or future prescription drug product candidates or non-prescription products, certain regulatory authorities will require that we report certain information about adverse medical events if those products may have caused or contributed to those adverse events. The timing of our obligation to report would be triggered by the date we become aware of the adverse event as well as the nature of the event. We may fail to report adverse events we become aware of within the prescribed timeframe. We may also fail to appreciate that we have become aware of a reportable adverse event, especially if such an event is not reported to us as an adverse event or if it is an adverse event that is unexpected or removed in time from the use of our products. If we fail to comply with our reporting obligations, the regulatory authorities could take action including, but not limited to, criminal prosecution, seizure of our products, facility inspections, removal of our products from the market, recalls of certain lots or batches, or cause a delay in approval or clearance of future products.

***Legislative or regulatory reforms with respect to animal health may make it more difficult and costly for us to obtain regulatory clearance or approval of any of our current or future product candidates and to produce, market, and distribute our products after clearance or approval is obtained.***

From time to time, legislation is drafted and introduced in the US Congress or other jurisdictions in which we intend to operate that could significantly change the statutory provisions governing the testing, regulatory clearance or approval, manufacture, and marketing of regulated products. In addition, the FDA's regulations and guidance are often revised or reinterpreted by the FDA and such other regulators in ways that may significantly affect our business and our products and product candidates. Similar changes in laws or regulations can occur in other countries. Any new regulations or revisions or reinterpretations of existing regulations in the US or in other countries may impose additional costs or lengthen review times of any of our current or future products and product candidates. We cannot determine what effect changes in regulations, statutes, legal interpretation or policies, when and if promulgated, enacted or adopted may have on our business in the future. Such changes could, among other things, require:

- changes to manufacturing methods;
- additional clinical trials or testing;
- new requirements related to approval to enter the market;
- recall, replacement, or discontinuance of certain products; and
- additional record keeping or the development of certain regulatory-required hazard identification plans.

Each of these would likely entail substantial time and cost and could harm our financial results. In addition, delays in receipt of or failure to receive regulatory clearances or approvals for any future products would harm our business, financial condition, and results of operations.

***We believe that our non-prescription products are not subject to regulation by regulatory agencies in the US, but there is a risk that regulatory bodies may disagree with our interpretation or may redefine the scope of their regulatory reach in the future, which would result in additional expense and could delay or prevent the commercialization of these products.***

The FDA retains jurisdiction over all animal prescription drug products. However, in many instances, the Federal Trade Commission will exercise primary or concurrent jurisdiction with the FDA on non-prescription products as to post-marketing claims made regarding the product. On April 22, 1996, the FDA published a statement in the Federal Register, 61 FR 17706, that it believes that the Dietary Supplement and Health Education Act ("DSHEA") does not apply to animal health supplement products, such as our non-prescription products. Accordingly, the FDA's Center for Veterinary Medicine only regulates those animal supplements that fall within the FDA's definition of an animal drug, animal food, or animal feed additive. The Federal Food Drug and Cosmetic Act defines food as "articles used for food or drinks for man or other animals and articles used as components of any such article." Animal foods are not subject to pre-market approval and are designed to provide a nutritive purpose to the animals that receive them. Feed additives are defined as those articles that are added to an animal's feed or water, as illustrated by the guidance documents. Our non-prescription products are not added to food, are not ingredients in food, nor are they added to any animal's drinking water. Therefore, our non-prescription products do not fall within the definition of a food or feed additive. In light of the pronouncement by the FDA that the DSHEA was not intended to apply to animals, the FDA seeks to regulate such supplements as food or food additives depending on the intended use of the product. The intended use is demonstrated by how the article is included in a food or added to the animals' intake (i.e., through its drinking water). If the intended use of the product does not fall within the proscribed use, making the product a food, it cannot be regulated as a food. There is no intent to make our non-prescription products a component of animal food, either directly or indirectly. A feed additive is a product that is added to a feed for any reason, including the top dressing of an already prepared feed. Some additives, such as certain forage, are deemed to be Generally Recognized as Safe, or GRAS, and therefore, not subject to a feed Additive Petition approval prior to use. However, the substances deemed GRAS are generally those that are recognized as providing nutrients as food does. We do not believe that our non-prescription products fit within this framework either. Finally, a new animal drug refers to drugs intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in animals. Our non-prescription Neonorm Foal and Neonorm Calf products are not intended to diagnose, cure, mitigate, treat, or prevent disease and, therefore, do not fit within the definition of an animal drug. Additionally, because a previously marketed human formulation of the botanical extract in our non-prescription products was regulated as a human dietary supplement subject to the DSHEA (and not regulated as a drug by the FDA), we do not believe that the FDA would regulate the animal formulation used in our non-prescription products in a different manner. We do not believe that our non-prescription products fit the definition of an animal drug, food, or food additive and, therefore, are not regulated by the FDA at this time.

However, despite many such unregulated animal supplements currently on the market, the FDA may choose in the future to exercise jurisdiction over animal supplement products, in which case, we may be subject to unknown regulations, thereby inhibiting our ability to launch or to continue marketing our non-prescription products. In the past, the FDA has redefined or attempted to redefine some non-prescription non-feed products as falling within the definition of drug, feed or feed additive and therefore subjected those products to the relevant regulations. We have not discussed with the FDA its belief that the FDA currently does not exercise jurisdiction over our non-prescription products. Should the FDA assert regulatory authority over our non-prescription products, we would take commercially reasonable steps to address the FDA's concerns, potentially including but not limited to seeking registration for such products, reformulating such products to further distance such products from regulatory control, or ceasing the sale of such products. Further, the Animal and Plant Health Inspection Service, an agency of the USDA, may at some point choose to exercise jurisdiction over certain non-prescription products that are not intended for production animals. We do not believe we are currently subject to such regulation but could be in the future. If the FDA or other regulatory agencies, such as the USDA, try to regulate our non-prescription products, we could be required to seek regulatory approval for our non-prescription products, which would result in additional expense and could delay or prevent the commercialization of these products.

***Even if we receive the required regulatory approvals for our current or future prescription drug product candidates and non-prescription products, we will be subject to ongoing obligations and continued regulatory review, which may result in significant additional expenses.***

If the FDA or any other regulatory body approves any of our current or future prescription drug product candidates, or if necessary, our non-prescription products, the manufacturing processes, clinical development, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion and recordkeeping for the product is subject to extensive and ongoing regulatory requirements. These requirements could include but are not limited to, submissions of efficacy and safety and other post-marketing information and reports, establishment registration, and product listing, compliance with new rules promulgated under the FSMA, as well as continued compliance with cGMPs, GLPs, and GCPs for any studies that Napo conducts post-approval. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with our contract manufacturers or manufacturing processes, or failure to comply with regulatory requirements, are reportable events to the FDA and may result in, among other things:

- restrictions on the marketing or manufacturing of the product, withdrawal of the product from the market, revised labeling, or voluntary or involuntary product recalls;
- additional clinical studies fines, warning letters or holds on studies;
- refusal by the FDA, or other regulators to approve pending applications or supplements to approved applications filed by Napo or Napo's strategic collaborators related to the unknown problems or suspension or revocation of the problematic product's license approvals;
- product seizure or detention, or refusal to permit the import or export of products; and
- injunctions or the imposition of civil or criminal penalties.

The FDA or other regulatory agency's policies may change, and additional government regulations may be enacted that could prevent, limit, or delay regulatory approval of our product candidates, require certain labeling changes, or require additional clinical work concerning the safety and efficacy of the product candidates. We cannot predict the likelihood, nature, or extent of government regulation that may arise from future legislation or administrative action, either in the US or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, and we may not achieve or sustain profitability, which would harm our business. In addition, failure to comply with these regulatory requirements could result in significant penalties.

In addition, from time to time, we may enter into consulting and other financial arrangements with physicians who prescribe or recommend our products once approved. As a result, we may be subject to state, federal, and foreign healthcare laws, including but not limited to anti-kickback laws. If our financial relationships with physicians or veterinarians are found to be in violation of such laws that apply to us, we may be subject to penalties.

#### **Risks Related to Our Common Stock**

***Our failure to meet the continued listing requirements of The Nasdaq Capital Market could result in a delisting of our common stock.***

Our common stock is listed on the Nasdaq Capital Market under the symbol "JAGX." In order to maintain that listing, we must satisfy minimum financial and other requirements, including, without limitation, the minimum stockholders' equity requirement and the minimum bid price requirement. There can be no assurances that we will be successful in maintaining, or if we fall out of compliance, in regaining compliance with the continued listing requirements and maintaining the listing of our common stock on the Nasdaq Capital Market. Delisting from Nasdaq could adversely affect our ability to raise additional financing through the public or private sale of equity securities,

and we would incur additional costs under requirements of state "blue sky" laws in connection with any sales of our securities. Delisting could also have other negative results, including the potential loss of confidence by employees, the loss of institutional investor interest, and fewer business development opportunities. If Nasdaq delists our common stock, the price of our common stock may decline, and our common stock may be eligible to trade on the OTC Bulletin Board, another over-the-counter quotation system, or on the pink sheets, which would negatively affect the liquidity of our common stock and an investor may find it more difficult to dispose of their common stock or obtain accurate quotations as to the market value of our common stock.

On January 23, 2023, we effected a 1-for-75 reverse stock split of our outstanding voting common stock. All share amounts and warrant or option exercise prices contained in this report reflect that adjustment. Additionally, in 2020, the SEC approved a Nasdaq rule change to expedite the delisting of securities of companies that have had one or more reverse stock splits with a cumulative ratio of one for 250 or more shares over the prior two-year period. Under the new rules, if a company falls out of compliance with the \$1.00 minimum bid price after completing reverse stock splits over the immediately preceding two years that cumulatively result in a ratio of one for 250 shares, the company will not be able to avail itself of any compliance periods. Nasdaq will instead require the issuance of a Staff delisting determination, which is appealable to a hearings panel. Our ability to remain listed on the Nasdaq Capital Market may be negatively impacted by this new Nasdaq rule.

We continue to actively monitor our performance with respect to the listing standards and will consider available options to resolve any deficiency and maintain compliance with the Nasdaq rules. There can be no assurance that we will be able to maintain compliance or, if we fall out of compliance, regain compliance with any deficiency, or if we implement an option that regains our compliance, maintain compliance thereafter.

***If our shares become subject to the penny stock rules, it would become more difficult to trade our shares.***

The SEC has adopted rules that regulate broker-dealer practices in connection with transactions in penny stocks. Penny stocks are generally equity securities with a price of less than \$5.00, other than securities registered on certain national securities exchanges or authorized for quotation on certain automated quotation systems, provided that current price and volume information with respect to transactions in such securities is provided by the exchange or system. If we do not retain a listing on The Nasdaq Capital Market and if the price of our common stock is less than \$5.00, our common stock will be deemed a penny stock. The penny stock rules require a broker-dealer, before a transaction in a penny stock not otherwise exempt from those rules, to deliver a standardized risk disclosure document containing specified information. In addition, the penny stock rules require that before effecting any transaction in a penny stock not otherwise exempt from those rules, a broker-dealer must make a special written determination that the penny stock is a suitable investment for the purchaser and receive (i) the purchaser's written acknowledgment of the receipt of a risk disclosure statement; (ii) a written agreement to transactions involving penny stocks and (iii) a signed and dated copy of a written suitability statement. These disclosure requirements may have the effect of reducing the trading activity in the secondary market for our common stock, and therefore, stockholders may have difficulty selling their shares.

***The price of our common stock could be subject to volatility related or unrelated to our operations, and purchasers of our common stock could incur substantial losses.***

We have experienced and may continue to experience significant volatility in the price of our common stock. From January 27, 2023, through January 26, 2024, the share price of our common stock ranged from a high of \$5.04 to a low of \$0.09. The reason for the volatility in our stock is not well understood and may continue. Factors that may have contributed to such volatility include but are not limited to, those discussed previously in this "Risk Factors" section of this report and others, such as:

- delays in the commercialization of Mytesi, Canalevia-CA1, or our other current or future prescription drug product candidates and non-prescription products;
- any delays in, or suspension or failure of, our current and future studies;

- announcements of regulatory approval or disapproval of any of our current or future product candidates or of regulatory actions affecting our company or our industry;
- manufacturing and supply issues that affect product candidate or product supply for our studies or commercialization efforts;
- quarterly variations in our results of operations or those of our competitors;
- changes in our earnings estimates or recommendations by securities analysts;
- the payment of licensing fees or royalties in shares of our common stock;
- announcements by us or our competitors of new prescription drug products or product candidates or non-prescription products, significant contracts, commercial relationships, acquisitions or capital commitments;
- announcements relating to future development or license agreements including termination of such agreements;
- adverse developments with respect to our intellectual property rights or those of our principal collaborators;
- commencement of litigation involving us or our competitors;
- any major changes in our board of directors or management;
- new legislation in the US relating to the prescription, sale, distribution or pricing of gastrointestinal health products;
- product liability claims, other litigation or public concern about the safety of our prescription drug product or product candidates and non-prescription products or any such future products;
- market conditions in the human or animal industry, in general, or in the gastrointestinal health sector, in particular, including performance of our competitors;
- future issuances of shares of common stock or other securities;
- uncertainties related to COVID-19;
- general economic conditions in the US and abroad; and
- market speculation regarding

In addition, the stock market, in general, or the market for stocks in our industry, in particular, may experience broad market fluctuations, which may adversely affect the market price or liquidity of our common stock. Any sudden decline in the market price of our common stock could trigger securities class-action lawsuits against us. If any of our stockholders were to bring such a lawsuit against us, we could incur substantial costs defending the lawsuit, and the time and attention of our management would be diverted from our business and operations. We also could be subject to damages claims if we were found to be at fault in connection with a decline in our stock price.

***A possible “short squeeze” due to a sudden increase in demand for our common stock that largely exceeds supply may lead to further price volatility in our common stock.***

Investors may purchase shares of our common stock to hedge existing exposure in our common stock or to speculate on the price of our common stock. Speculation on the price of our common stock may involve long and short exposures. To the extent aggregate short exposure exceeds the number of shares of our common stock available for purchase in the open market, investors with short exposure may have to pay a premium to repurchase our common stock for delivery to lenders of our common stock. Those repurchases may dramatically increase the price of our common stock until investors with short exposure can purchase additional shares of common stock to cover their short position. This is often referred to as a “short squeeze.” A short squeeze could lead to volatile price movements in shares of our common stock that are not directly correlated to our company’s performance or prospects. Once investors purchase the shares necessary to cover their short position, the price of our common stock may decline.

***You may not be able to resell our common stock when you wish to sell it or at a price that you consider attractive or satisfactory.***

The listing of our common stock on The Nasdaq Capital Market does not assure that a meaningful, consistent, and liquid trading market exists. Although our common stock is listed on The Nasdaq Capital Market, its trading volume has been limited, and an active trading market for our shares may never develop or be sustained. If an active market for our common stock does not develop, you may be unable to sell your shares when you wish to sell them or at a price that you consider attractive or satisfactory. The lack of an active market may also adversely affect our ability to raise capital by selling securities in the future or impair our ability to license or acquire other product candidates, businesses, or technologies using our shares as consideration.

***If securities or industry analysts do not publish research or reports about our company, or if they issue adverse or misleading opinions regarding us or our stock, our stock price and trading volume could decline.***

The trading market for our common stock depends in part on the research and reports that industry or financial analysts publish about us or our business. We do not influence or control the reporting of these analysts. If one or more of the analysts who do cover us downgrade or provide a negative outlook on our company, our industry, or the stock of any of our competitors, the price of our common stock could decline. If one or more of these analyst’s ceases coverage of our company, we could lose visibility in the market, which in turn could cause the price of our common stock to decline.

***You may be diluted by conversions of outstanding shares of non-voting common stock, exercises of outstanding options and warrants, and issuances of securities pursuant to our ATM Agreement.***

As of December 31, 2023, we had (i) outstanding options to purchase an aggregate of 26,262 shares of our common stock at a weighted average exercise price of \$599.12 per share, (ii) outstanding options to purchase an aggregate of 1,512 shares of our common stock issuable upon exercise of outstanding inducement options, with a weighted-average exercise price of \$346.17 per share, (iii) 11,424,807 shares of our common stock issuable upon exercise of warrants outstanding, with weighted-average exercise price of \$538.5, (iv) 2,708,136 shares of our common stock issuable upon vesting of outstanding RSUs, (v) 37,237 shares of our common stock issuable to third parties upon exercise of those shares, and (vi) 9 shares of our non-voting common stock issuable at an equivalent share of voting common stock. The exercise of such options, warrants, vesting of RSUs, and conversion of the non-voting common stock will result in further dilution of your investment.

In addition, you may experience further dilution if we issue common stock in the future, including common stock issued pursuant to our existing At The Market Offering Agreement (the “ATM Agreement”). Pursuant to the ATM Agreement with Ladenburg Thalmann & Co. Inc. (“Ladenburg”), we may offer and sell up to \$75.0 million of our common stock from time to time through Ladenburg as our sales agent. During the year ended December 31, 2023, we sold 55,222,089 shares of common stock pursuant to the ATM Agreement for net proceeds of \$32.1 million.

As a result of this dilution, you may receive significantly less in net tangible book value than the full purchase price you paid for the shares in the event of liquidation.

***Provisions in our charter documents and under Delaware law could discourage a takeover that stockholders may consider favorable and may lead to entrenchment of management.***

Our third amended and restated certificate of incorporation and amended and restated bylaws contain provisions that could delay or prevent changes in control or changes in our management without the consent of our board of directors. These provisions include the following:

- a classified board of directors with three-year staggered terms, which may delay the ability of stockholders to change the membership of a majority of our board of directors;
- no cumulative voting in the election of directors, which limits the ability of minority stockholders to elect director candidates;
- the exclusive right of our board of directors to elect a director to fill a vacancy created by the expansion of the board of directors or the resignation, death or removal of a director, which prevents stockholders from being able to fill vacancies on our board of directors;
- the ability of our board of directors to authorize the issuance of shares of preferred stock and to determine the terms of those shares, including preferences and voting rights, without stockholder approval, which could adversely affect the rights of our common stockholders or be used to deter a possible acquisition of our company;
- the ability of our board of directors to alter our bylaws without obtaining stockholder approval;
- the required approval of the holders of at least 75% of the shares entitled to vote at an election of directors to adopt, amend, or repeal our bylaws or repeal the provisions of our third amended and restated certificate of incorporation regarding the election and removal of directors;
- a prohibition on stockholder action by written consent, which forces stockholder action to be taken at an annual or special meeting of our stockholders;
- the requirement that a special meeting of stockholders may be called only by the chairman of the board of directors, the chief executive officer, the president, or the board of directors, which may delay the ability of our stockholders to force consideration of a proposal or to take action, including the removal of directors; and
- advance notice procedures that stockholders must comply with in order to nominate candidates to our board of directors or to propose matters to be acted upon at a stockholders' meeting, which may discourage or deter a potential acquirer from conducting a solicitation of proxies to elect the acquirer's own slate of directors or otherwise attempting to obtain control of us.

These provisions could inhibit or prevent possible transactions that some stockholders may consider attractive.

We are also subject to the anti-takeover provisions contained in Section 203 of the Delaware General Corporation Law. Under Section 203, a corporation generally may not engage in a business combination with any holder of 15% or more of its capital stock unless the holder has held the stock for three years or, among other exceptions, the board of directors has approved the transaction.

***Our amended and restated bylaws designate the Court of Chancery of the State of Delaware as the sole and exclusive forum for certain actions and proceedings that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or other employees.***

Our amended and restated bylaws provide that unless we consent in writing to an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a claim of breach of a fiduciary duty owed by any director, officer or other employee to us or our stockholders, (iii) any action asserting a claim arising pursuant to any provision of the Delaware General Corporation Law, (iv) any action asserting a claim that is governed by the internal affairs doctrine or (v) any action to interpret, apply, enforce or determine the validity of our certificate of incorporation or bylaws. Any person purchasing or otherwise acquiring any interest in any shares of our capital stock shall be deemed to have notice of and to have consented to this provision of our amended and restated bylaws. This choice-of-forum provision may limit our stockholders' ability to bring a claim in a judicial forum that they find favorable for disputes with us or our directors, officers, or other employees, which may discourage such lawsuits. Alternatively, if a court were to find this provision of our amended and restated bylaws inapplicable or unenforceable with respect to one or more of the specified types of actions or proceedings, we may incur additional costs associated with resolving such matters in other jurisdictions, which could harm our business and financial condition.

***We do not intend to pay dividends on our common stock, and your ability to achieve a return on your investment will depend on appreciation in the market price of our common stock.***

We currently intend to invest our future earnings, if any, to fund our growth and not to pay any cash dividends on our common stock. Because we do not intend to pay dividends, your ability to receive a return on your investment will depend on any future appreciation in the market price of our common stock. We cannot be certain that our common stock will appreciate in price.

***The requirements of being a public company, including compliance with the reporting requirements of the Exchange Act and the requirements of the Sarbanes-Oxley Act, may strain our resources, increase our costs, and distract management, and we may be unable to comply with these requirements in a timely or cost-effective manner.***

Our initial public offering had a significant, transformative effect on us. Prior to our initial public offering, our business operated as a privately held company, and we were not required to comply with public reporting, corporate governance, and financial accounting practices and policies required of a publicly traded company. As a publicly traded company, we incur significant additional legal, accounting, and other expenses compared to historical levels. In addition, new and changing laws, regulations, and standards relating to corporate governance and public disclosure, including the Dodd-Frank Wall Street Reform and Consumer Protection Act and the rules and regulations thereunder, as well as under the Sarbanes-Oxley Act, the JOBS Act and the rules and regulations of the SEC and The Nasdaq Capital Market, may result in an increase in our costs and the time that our board of directors and management must devote to our compliance with these rules and regulations. These rules and regulations have substantially increased our legal and financial compliance costs and diverted management time and attention from our product development and other business activities.

The Sarbanes-Oxley Act requires, among other things, that we assess the effectiveness of our internal control over financial reporting annually and the effectiveness of our disclosure controls and procedures quarterly. In particular, Section 404 of the Sarbanes-Oxley Act, or Section 404, requires us to perform system and process evaluation and testing of our internal control over financial reporting to allow management to report on and our independent registered public accounting firm potentially to attest to the effectiveness of our internal control over financial reporting. We have needed to expend time and resources on documenting our internal control over financial reporting so that we are in a position to perform such evaluation when required. As a smaller reporting company ("SRC"), we expect to avail ourselves of the exemption from the requirement that our independent registered public accounting firm attest to the effectiveness of our internal control over financial reporting under Section 404. However, we may no longer avail ourselves of this exemption when we cease to be an SRC. When our independent registered

public accounting firm is required to undertake an assessment of our internal control over financial reporting, the cost of our compliance with Section 404 will correspondingly increase. Our compliance with applicable provisions of Section 404 requires that we incur substantial accounting expenses and expend significant management time on compliance-related issues as we implement additional corporate governance practices and comply with reporting requirements. Moreover, if we are not able to comply with the requirements of Section 404 applicable to us in a timely manner, or if we or our independent registered public accounting firm identify deficiencies in our internal control over financial reporting that are deemed to be material weaknesses, the market price of our stock could decline, and we could be subject to sanctions or investigations by the SEC or other regulatory authorities, which would require additional financial and management resources.

***We are a smaller reporting company and the reduced reporting requirements applicable to smaller reporting companies may make our common stock less attractive to investors.***

We are a smaller reporting company ("SRC") and a non-accelerated filer, which allows us to take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not SRCs or non-accelerated filers, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, as amended, reduced disclosure obligations regarding executive compensation in our Annual Report and our periodic reports and proxy statements and providing only two years of audited financial statements in our Annual Report and our periodic reports. We will remain an SRC so long as (a) the aggregate market value of our outstanding common stock held by non-affiliates as of the last business day our most recently completed second fiscal quarter is less than \$250 million or (b) (1) we have less than \$100 million in annual revenues and (2) the aggregate market value of our outstanding common stock held by non-affiliates as of the last business day our most recently completed second fiscal quarter is less than \$700 million. We cannot predict whether investors will find our common stock less attractive if we rely on certain or all of these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock, and our stock price may be more volatile and may decline.

**ITEM 1B. UNRESOLVED STAFF COMMENTS**

None.

**ITEM 1C. CYBERSECURITY**

**Risk management and strategy**

We have established policies and processes for assessing, identifying, and managing material risk from cybersecurity threats and have integrated these processes into our overall risk management systems and processes. We routinely assess material risks from cybersecurity threats, including any potential unauthorized occurrence on or conducted through our information systems that may result in adverse effects on the confidentiality, integrity, or availability of our information systems or any information residing therein.

We conduct periodic risk assessments to identify cybersecurity threats, as well as assessments in the event of a material change in our business practices that may affect information systems that are vulnerable to such cybersecurity threats. These risk assessments include the identification of reasonably foreseeable internal and external risks, the likelihood and potential damage that could result from such risks, and the sufficiency of existing policies, procedures, systems, and safeguards in place to manage such risks.

Following these risk assessments, we re-design, implement, and maintain reasonable safeguards to minimize identified risks, reasonably address any identified gaps in existing safeguards, and regularly monitor the effectiveness of our safeguards. Primary responsibility for assessing, monitoring, and managing our cybersecurity risks rests with an IT consultant who reports to our Chief Compliance Officer to manage the risk assessment and mitigation process.

As part of our overall risk management system, we monitor and test our safeguards and train our employees on these safeguards in collaboration with IT and management. Personnel at all levels and departments are made aware of our cybersecurity policies through training sessions.

We engage consultants or other third parties in connection with our risk assessment processes. These service providers assist us in designing and implementing our cybersecurity policies and procedures and monitor and test our safeguards. We require each third-party service provider to certify that it has the ability to implement and maintain appropriate security measures, consistent with all applicable laws, to implement and maintain reasonable security measures in connection with their work with us, and to promptly report any suspected breach of its security measures that may affect our company.

We have not encountered cybersecurity challenges that have materially impaired our operations or financial standing. For additional information regarding risks from cybersecurity threats, please refer to Item 1A, "Risk Factors," in this annual report on Form 10-K.

#### **Governance**

One of the key functions of our board of directors is informed oversight of our risk management process, including risks from cybersecurity threats. Our board of directors is responsible for monitoring and assessing strategic risk exposure, and our executive officers are responsible for the day-to-day management of the material risks we face. Our board of directors administers its cybersecurity risk oversight function directly as a whole, as well as through the audit committee.

Our Chief Financial Officer and Chief Compliance Officer are primarily responsible for assessing and managing our material risks from cybersecurity threats with assistance from third-party service providers.

Our Chief Financial Officer and Chief Compliance Officer oversee our cybersecurity policies and processes, including those described in "Risk Management and Strategy" above. The cybersecurity risk management program includes tools and activities to prevent, detect, and analyze current and emerging cybersecurity threats and plans and strategies to address threats and incidents.

Our Chief Compliance Officer and IT consultant provide periodic briefings to the audit committee regarding our company's cybersecurity risks and activities, including any recent cybersecurity incidents and related responses, cybersecurity systems testing, activities of third parties, and the like. Our audit committee provides regular updates to the board of directors on such reports.

#### **ITEM 2. PROPERTIES**

Our corporate headquarters are located at 200 Pine Street, Suite 400, San Francisco, California.

#### **ITEM 3. LEGAL PROCEEDINGS**

From time to time, we may be subject to various legal proceedings and claims that arise in the ordinary course of our business activities. Regardless of the outcome, litigation can have a material adverse effect on us due to defense and settlement costs, diversion of our management resources, and other factors. We are not currently subject to any material legal proceedings.

#### **ITEM 4. MINE SAFETY DISCLOSURE**

Not applicable.

## PART II

### ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES

#### Market Information

Our common stock trades on The Nasdaq Capital Market under the symbol "JAGX."

#### Holders

As of April 1, 2025, there were approximately 22 stockholders of record of our common stock. These figures do not reflect the beneficial ownership or shares held in the nominee's name nor include holders of any RSUs.

#### Dividend Policy

We have never paid any cash dividends on our common stock to date. We currently anticipate that we will retain all future earnings, if any, to fund the development and growth of our business and do not anticipate paying any cash dividends for at least the next five years, if ever.

#### Recent Sales of Unregistered Securities

On December 28, 2023, pursuant to that certain exchange agreement dated December 28, 2023, the Company issued 4,875,000 shares of the Company's common stock to Iliad Research and Trading, L.P. in exchange for a \$785,362.50 reduction in the outstanding balance of the royalty interest held by Iliad Research and Trading, L.P.

Other than equity securities issued in transactions disclosed above and on our Current Report on Form 8-K filed with the SEC on October 5, 2023, there were no unregistered sales of equity securities during the period. Refer to Item 15. Subsequent Events for subsequent sales of unregistered securities.

The offers, sales, and issuances of the securities described above were deemed to be exempt from registration under the Securities Act in reliance on Section 3(a)(9) of the Securities Act, Section 4(a)(2) of the Securities Act, or Regulation D or Regulation S promulgated thereunder as transactions by an issuer not involving a public offering. The recipients of securities in each of these transactions acquired the securities for investment only and not with a view to or for sale in connection with any distribution thereof, and appropriate legends were affixed to the securities issued in these transactions. Each of the recipients of securities in these transactions was an accredited or sophisticated person and had adequate access, through employment, business, or other relationships, to information about us.

### ITEM 6. SELECTED FINANCIAL DATA

Not Applicable.

### ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

*The following discussion and analysis should be read together with our financial statements and the related notes appearing elsewhere in this report.*

#### Overview

Jaguar Health, Inc. ("Jaguar" or the "Company") is a commercial stage pharmaceuticals company focused on developing novel, plant-based, sustainably derived prescription medicines for people and animals with gastrointestinal ("GI") distress, including chronic, debilitating diarrhea. Jaguar Health's wholly owned subsidiary, Napo

Pharmaceuticals, Inc. ("Napo"), focuses on developing and commercializing proprietary plant-based human pharmaceuticals from plants harvested responsibly from rainforest areas. Our crofelemer drug product candidate is the subject of the OnTarget study, a pivotal Phase 3 clinical trial for prophylaxis of diarrhea in adult cancer patients receiving targeted therapy. Jaguar is the majority stockholder of Napo Therapeutics S.p.A. ("Napo Therapeutics"), an Italian corporation established by Jaguar in Milan, Italy, in 2021 that focuses on expanding crofelemer access in Europe. Napo Therapeutics' core mission is to provide access to crofelemer in Europe to address significant rare/orphan disease indications, including, initially, two key rare disease target indications: Short bowel syndrome ("SBS") with intestinal failure, rare disease indications of microvillus inclusion disease ("MVID") and/or congenital diarrheal disorders ("CDD"). Jaguar Animal Health is a trademark of Jaguar Health.

Jaguar was founded in San Francisco, California as a Delaware corporation on June 6, 2013 (inception). The Company was a majority-owned subsidiary of Napo until the close of the Company's initial public offering on May 18, 2015. The Company was formed to develop and commercialize first-in-class prescription and non-prescription products for companion animals.

On July 31, 2017, Jaguar completed a merger with Napo pursuant to the Agreement and Plan of Merger dated March 31, 2017, by and among Jaguar, Napo, Napo Acquisition Corporation ("Merger Sub"), and Napo's representative (the "Merger Agreement"). In accordance with the terms of the Merger Agreement, upon the completion of the merger, Merger Sub merged with and into Napo, with Napo surviving as the wholly owned subsidiary (the "Merger" or "Napo Merger"). Immediately following the Merger, Jaguar changed its name from "Jaguar Animal Health, Inc." to "Jaguar Health, Inc." Napo now operates as a wholly owned subsidiary of Jaguar focused on human health including the ongoing development of crofelemer and commercialization of Mytesi.

Napo's marketed drug Mytesi (crofelemer 125 mg delayed-release tablets) is a first-in-class oral botanical drug product approved by the US Food and Drug Administration ("FDA") for the symptomatic relief of noninfectious diarrhea in adults with HIV/AIDS on antiretroviral therapy. To date, this is the only oral plant-based botanical prescription medicine approved under the FDA's Botanical Guidance. The Company's Canalevia-CA1 (crofelemer delayed-release tablets) drug is the first and only oral plant-based prescription product that is FDA conditionally approved to treat chemotherapy-induced diarrhea ("CID") in dogs.

Crofelemer was granted ODD by the FDA in February 2023 for MVID, an ultrarare CDD condition, and granted ODD for MVID by the European Medicines Agency ("EMA") in October 2022. Crofelemer was granted ODD for SBS by the EMA in December 2021 and by the FDA in August 2017. In 2024 Jaguar expects results from 5 proof-of-concept studies of crofelemer conducted at least 8 clinical sites, including Cleveland Clinic, on three continents for the rare disease indications of MVID – an ultrarare CDD and SBS. In accordance with the guidelines of specific European Union countries, published data from such clinical investigations could support reimbursed early patient access to crofelemer for these debilitating conditions in 2025 while the company pursues approval of crofelemer for SBS and MVID from the EMA and the FDA. In August 2023 the FDA activated Napo's Investigational New Drug ("IND") application for a new crofelemer powder for oral solution formulation for the treatment of MVID.

SBS affects approximately 10,000 to 20,000 people in the US, according to the Crohn's & Colitis Foundation, and it is estimated that the population of SBS patients in Europe is approximately the same size. Despite limited treatment options, the global SBS market exceeded \$568 million in 2019 and is expected to reach \$4.6 billion by 2027, according to a report by Vision Research Reports.

Most of the activities of the Company are focused on the development and/or commercialization of Mytesi, including the ongoing clinical development of crofelemer for the prophylaxis of diarrhea in adult patients receiving targeted cancer therapy, and our prioritized clinical program centered around the approved investigator-initiated POC trial of crofelemer for SBS and CDD. Napo's pivotal OnTarget Phase 3 clinical trial of crofelemer for prophylaxis of cancer therapy-related diarrhea ("CTD") was initiated in October 2020.

In the field of animal health, we are continuing limited activities related to developing and commercializing first-in-class gastrointestinal products for dogs, dairy calves and foals.

Crofelemer is a novel, first-in-class anti-secretory antidiarrheal drug which has a normalizing effect on electrolyte and fluid balance in the gut, and this mechanism of action has the potential to benefit multiple disorders that cause gastrointestinal distress, including diarrhea and abdominal discomfort. Mytesi is in development for multiple possible follow-on indications, including prophylaxis of diarrhea related to targeted therapy with or without standard chemotherapy. Crofelemer delayed-release tablets are also being evaluated in diarrhea-predominant irritable bowel syndrome ("IBS-D") and idiopathic/functional diarrhea.

Crofelemer powder for oral solution is being developed to support orphan or rare disease indications for infants and/or children with SBS and/or CDD, such as MVID.

In addition, a second-generation proprietary anti-secretory antidiarrheal drug ("NP-300") is in development for symptomatic relief and treatment of moderate-to-severe diarrhea, with or without concomitant antimicrobial therapy, from bacterial, viral and parasitic infections including *Vibrio cholerae*, the bacterium that causes cholera.

In December 2021 we received conditional approval from the FDA to market Canalevia-CA1 (crofelemer delayed-release tablets), our oral plant-based prescription drug and the only available veterinary drug for the treatment of chemotherapy-induced diarrhea ("CID") in dogs, and Canalevia-CA1 is now available to multiple leading veterinary distributors in the US. Canalevia-CA1 is a tablet that is given orally and can be prescribed for home treatment of CID. Canalevia-CA1 is conditionally approved by the FDA under application number 141-552. Conditional approval allows for commercialization of the product while Jaguar Animal Health continues to collect the substantial evidence of effectiveness required for full approval. We have received Minor Use in a Major Species ("MUMS") designation from the FDA for Canalevia-CA1 to treat CID in dogs. FDA has established a "small number" threshold for minor use in each of the seven major species covered by the MUMS act. The small number threshold is currently 80,000 for dogs, representing the largest number of dogs that can be affected by a disease or condition over the course of a year and still have the use qualify as a minor use.

In January 2023, Jaguar and Filament Health ("Filament"), with funding from One Small Planet, formed the US-based joint venture Magdalena Biosciences, Inc. ("Magdalena"). Magdalena's focus is on the development of novel, natural prescription medicines derived from plants for mental health indications including, initially, attention-deficit/hyperactivity disorder ("ADHD") in adults. The goal of the collaboration is to extend the botanical drug development capabilities of Jaguar and Filament in order to develop pharmaceutical-grade, standardized drug candidates for mental health disorders, and to partner with a potential future licensee to develop and commercialize these novel plant-based drugs. This new venture aligns with Jaguar's mental health Entheogen Therapeutics Initiative ("ETI") and Filament's corporate mission to develop novel, natural prescription medicines from plants. Magdalena will leverage Jaguar's proprietary medicinal plant library and Filament's proprietary drug development technology. Jaguar's library of 2,300 highly characterized medicinal plants and 3,500 plant extracts, all from firsthand ethnobotanical investigation by Jaguar and members of the ETI Scientific Strategy Team, is a key asset we have generated over 30 years that bridges the knowledge of traditional healers and Western medicine. Magdalena holds an exclusive license to plants and plant extracts in Jaguar's library, not including any sources of crofelemer or NP-300, for specific indications and is in the process of identifying plant candidates in the library that may prove beneficial for addressing indications such as ADHD.

We believe Jaguar is poised to realize a number of synergistic, value adding benefits—an expanded pipeline of potential blockbuster human follow-on indications of crofelemer, and a second-generation anti-secretory agent—upon which to build global partnerships. Jaguar, through Napo, holds global unencumbered rights for crofelemer, Mytesi, and Canalevia-CA1. Additionally, several of the drug product opportunities in Jaguar's crofelemer pipeline are backed by Phase 2 and proof of concept evidence from human clinical trials.

## Financial Operations Overview

On a consolidated basis, we have not yet generated enough revenue to date to achieve break-even or positive cash flow, and we expect to continue to incur significant research and development and other expenses. Our net comprehensive losses were \$41.9 million and \$49.1 million for the years ended December 31, 2023 and 2022, respectively. As of December 31, 2023, we had total stockholders' equity of \$4.9 million, an accumulated deficit of \$308.2 million, an accumulated other comprehensive loss of \$652,000 and cash of \$6.5 million. We expect to continue to incur losses and experience increased expenditures for the foreseeable future as we expand our product development activities, seek necessary approvals for our product candidates, conduct species-specific formulation studies for our non-prescription products, establish active pharmaceutical ingredient ("API") manufacturing capabilities and begin additional commercialization activities.

### **Revenue**

Our product and collaboration revenue consists of the following:

- Revenues from the sale of our human drug Mytesi, which is sold through distributors and wholesalers and specialty pharmacies.
- Revenues from the sale of our animal products branded as Canalevia-CA1, Neonorm Calf and Neonorm Foal. Our Canalevia-CA1, Neonorm and botanical extract products are primarily sold to distributors, who then sell the products to the end customers.
- Our policy typically permits returns if the product is damaged, defective, or otherwise cannot be used when received by the customer if the product has expired. Returns are accepted for product that will expire within six months or that have expired up to one year after their expiration dates. Estimates for expected returns of expired products are based primarily on an ongoing analysis of our historical return patterns.

See "Results of Operations" below for more detailed discussion on revenues.

### **Cost of Revenue**

Cost of revenue consists of direct drug substance and drug product materials expense, direct labor, distribution fees, royalties and other related expenses associated with the sale of our products.

### **Research and Development Expense**

Research and development expenses consist primarily of clinical and contract manufacturing expense, personnel and related benefit expense, stock-based compensation expense, employee travel expense and reforestation expenses. Clinical and contract manufacturing expense consists primarily of costs to conduct stability, safety and efficacy studies, and manufacturing startup expenses at an outsourced API provider in Italy. It also includes expenses with a third-party provider for the transfer of the Mytesi manufacturing process, and the related feasibility and validation activities.

We typically use our employee and infrastructure resources across multiple development programs. We track outsourced development costs by prescription drug product candidate and non-prescription product but do not allocate personnel or other internal costs related to development to specific programs or development compounds.

The timing and amount of our research and development expenses will depend largely upon the outcomes of current and future trials for our prescription drug product candidates as well as the related regulatory requirements, the outcomes of current and future species-specific formulation studies for our non-prescription products, manufacturing

costs and any costs associated with the advancement of our line extension programs. We cannot determine with certainty the duration and completion costs of the current or future development activities.

The duration, costs and timing of trials, formulation studies and development of our prescription drug and non-prescription products will depend on a variety of factors, including:

- the scope, rate of progress, and expense of our ongoing, as well as any additional clinical trials, formulation studies and other research and development activities;
- future clinical trial and formulation study results;
- potential changes in government regulations; and
- the timing and receipt of any regulatory approvals.

A change in the outcome of any of these variables with respect to the development of a prescription drug product candidate or non-prescription product could mean a significant change in the costs and timing associated with our development activities.

We expect research and development expense to increase due to the start-up costs associated with our clinical trials for other indications.

#### ***Sales and Marketing Expense***

Sales and marketing expenses consist of personnel and related benefit expense, stock- based compensation expense, direct sales and marketing expense, employee travel expense, and management consulting expense. We currently incur sales and marketing expenses to promote Mytesi. We do not currently have any marketing or promotional expenses related to Canalevia-CA1, Neonorm Calf or Neonorm Foal for the years ended December 31, 2023 and 2022.

We expect sales and marketing expense to increase going forward as we focus on expanding our market access activities and commercial partnerships for the development of follow-on indications of Mytesi and crofelemer.

#### ***General and Administrative Expense***

General and administrative expenses consist of personnel and related benefit expense, stock-based compensation expense, employee travel expense, legal and accounting fees, rent and facilities expense, and management consulting expense.

In the near term, we expect general and administrative expense to remain flat as we focus on our pipeline development and market access expansion. This will include efforts to grow the business.

#### ***Interest Expense***

Interest expense consists primarily of non-cash and cash interest costs related to our borrowings.

#### ***Change in Fair Value of Financial Instruments and Hybrid Instrument Designated at Fair Value Option***

Change in fair value of freestanding and hybrid financial instruments designated at Fair Value Option consists of gain or loss recognized related to fair values changes of our instruments designated at FVO.

**Gain (Loss) on Debt Extinguishment**

Gain (loss) on debt extinguishment consists of gain or loss incurred related to the exchanges resulting from the extinguishment of our borrowings.

**Critical Accounting Policies and Significant Judgments and Estimates**

The preparation of financial statements in conformity with US generally accepted accounting principles ("US GAAP") requires the use of estimates and assumptions that affect the reported amounts of assets and liabilities, revenues and expenses, and related disclosures in the financial statements. Critical accounting policies are those accounting policies that may be material due to the levels of subjectivity and judgment necessary to account for highly uncertain matters or the susceptibility of such matters to change, and that have a material impact on financial condition or operating performance. While we base our estimates and judgments on our experience and on various other factors that we believe to be reasonable under the circumstances, actual results may differ from these estimates under different assumptions or conditions. We believe the following critical accounting policies used in the preparation of our financial statements require significant judgments and estimates. For additional information relating to these and other accounting policies, see Note 2 to the consolidated financial statements, appearing elsewhere in this report.

**Results of Operations****Comparison of the Years Ended December 31, 2023 and 2022**

The following table summarizes the Company's results of operations with respect to the items set forth in such table for the years ended December 31, 2023 and 2022 together with the change in such items in dollars and as a percentage.

(in thousands)	Year Ended December 31,		Variance	Variance %
	2023	2022		
Product revenue, net	\$ 9,761	\$ 11,956	\$ (2,195)	(18.4)%
Operating Expenses				
Cost of product revenue	2,037	2,019	18	0.9 %
Research and development	18,596	17,647	949	5.4 %
Sales and marketing	6,460	8,837	(2,377)	(26.9)%
General and administrative	16,588	17,868	(1,280)	(7.2)%
Impairment loss on intangible assets	371	—	371	100.0 %
Total operating expenses	44,052	46,371	(2,319)	(5.0)%
Loss from operations	(34,291)	(34,415)	124	(0.4)%
Interest expense	(6,382)	(12,723)	6,341	(49.8)%
Change in fair value of freestanding and hybrid financial instruments designated at Fair Value Option	(5,125)	(20)	(5,105)	25,525.0 %
Gain (loss) on extinguishment of debt	3,697	(2,187)	5,884	(269.0)%
Other income	200	950	(750)	(78.9)%
Loss before income tax	(41,901)	(48,395)	6,494	(13.4)%
Income tax expense	—	—	—	100.0 %
Net loss	\$ (41,901)	\$ (48,395)	\$ 6,494	(13.4)%
Net loss attributable to noncontrolling interest	\$ (601)	\$ (941)	\$ 340	(36.1)%
Net loss attributable to common stockholders	\$ (41,300)	\$ (47,454)	\$ 6,154	(13.0)%

**Revenue**

*Product revenue*

Sales discounts were \$1.4 million and \$1.2 million for the years ended December 31, 2023, and 2022, respectively, an increase of \$267,000.

Medicaid and AIDS Drug Assistance Program ("ADAP") rebates accounted for \$2.0 million and \$1.8 million for the years ended December 31, 2023 and 2022, respectively, an increase of \$205,000.

Due to the Company's arrangements, including elements of variable consideration, gross product sales are reduced in order to reflect the expected consideration to arrive at net product sales. Deductions to reduce gross product sales to net product sales for the years ended December 31, 2023 and 2022 are as follows:

(in thousands)	Year Ended December 31,		Variance	Variance %
	2023	2022		
Gross product sales				
Mytesi	\$ 13,435	\$ 14,804	\$ (1,369)	(9.2)%
Canalevia	130	167	(37)	(22.2)%
Neonorm	42	48	(6)	(12.5)%
Total gross product sales	13,607	15,019	(1,412)	(9.4)%
Medicaid rebates	(2,041)	(1,836)	(205)	11.2 %
Sales discounts	(1,449)	(1,182)	(267)	22.6 %
Sales returns	(356)	(45)	(311)	691.1 %
Net product sales	<u>\$ 9,761</u>	<u>\$ 11,956</u>	<u>\$ (2,195)</u>	<u>(18.4)%</u>

Our gross product revenues were \$13.6 million and \$15.0 million for the years ended December 31, 2023 and 2022, respectively. These figures reflect revenue from the sale of our human drug Mytesi, our animal products branded as Neonorm Calf and Neonorm Foal.

Our Mytesi product revenues were \$13.4 million and \$14.8 million for the years ended December 31, 2023 and 2022, respectively. Our Canalevia product revenues were \$130,000 and \$167,000 for the years ended December 31, 2023 and 2022, respectively. Our Neonorm product revenues were \$42,000 and \$48,000 for the years ended December 31, 2023 and 2022, respectively. Sales and marketing expenses are not significant during 2023 and during the same period in 2022.

*Cost of Product Revenue*

(in thousands)	Year Ended December 31,		Variance	Variance %
	2023	2022		
Cost of Product Revenue				
Direct labor	\$ 1,152	\$ 755	\$ 397	52.6 %
Material cost	885	1,011	(126)	(12.5)%
Royalties	—	54	(54)	(100.0)%
Distribution fees	(49)	15	(64)	(426.7)%
Other	49	184	(135)	(73.4)%
Total	<u>\$ 2,037</u>	<u>\$ 2,019</u>	<u>\$ 18</u>	<u>0.9 %</u>

The change in cost of product revenue of \$18,000 for the year ended December 31, 2023 compared to 2022 was primarily due to:

- Direct labor increased \$397,000 from \$755,000 for the year ended December 31, 2022 to \$1.2 million in 2023, due to increased resources in testing and manufacturing.
- Material cost decreased by \$126,000 from \$1.0 million for the year ended December 31, 2022, to \$885,000 in 2023 relative to the decrease in net sales.
- Other costs which includes royalties and APIs decreased \$135,000 from \$184,000 for the year ended December 31, 2022 to \$49,000 in 2023 relative to the decrease in net sales.

*Research and Development Expense*

The following table presents the components of research and development ("R&D") expense for the years ended December 31, 2023 and 2022:

(in thousands)	Year Ended December 31,		Variance	Variance %
	2023	2022		
<i>Research and Development:</i>				
Clinical and contract manufacturing	\$ 8,155	\$ 8,326	\$ (171)	(2.1)%
Personnel and related benefits	5,815	5,543	272	4.9 %
Stock-based compensation	1,044	1,263	(219)	(17.3)%
Materials expense and tree planting	367	309	58	18.8 %
Travel and other expenses	326	122	204	167.2 %
Other	2,889	2,084	805	38.6 %
Total	\$ 18,596	\$ 17,647	\$ 949	5.4 %

The change in R&D expense of \$949,000 for the year ended December 31, 2023 compared to 2022 was primarily due to:

- Clinical and contract manufacturing expenses decreased \$171,000 from \$8.3 million for the year ended December 31, 2022 to \$8.2 million in 2023 largely due to lower clinical trial activities related to start-up of CTD and other indications, additional CMC manufacturing, consulting and contractors' expenses, and cholera/lechlemer research expenses.
- Personnel and related benefits increased \$272,000 from \$5.5 million for the year ended December 31, 2022 to \$5.8 million in 2023 largely due an increase in headcount.
- Stock-based compensation expense decreased \$219,000 from \$1.3 million for the year ended December 31, 2022 to \$1.0 million in 2023 primarily due to lower options and RSUs granted during the period as compared to 2022.
- Travel, and other expenses increased by \$204,000 from \$122,000 for the year ended December 31, 2022 to \$326,000 in 2023 primarily due to more travel activities associated with the clinical trials.
- Other expenses consisting of consulting, formulation and regulatory fees increased \$805,000 from \$2.1 million for the year ended December 31, 2022, to \$2.9 million in 2023 mainly due to increased CTD activities.

***Sales and Marketing Expense***

The following table presents the components of sales and marketing ("S&M") expense for the years ended December 31, 2023 and 2022:

(in thousands)	Year Ended December 31,		Variance	Variance %
	2023	2022		
<b><i>Sales and Marketing:</i></b>				
Personnel and related benefits	\$ 3,025	\$ 3,415	\$ (390)	(11.4)%
Direct marketing fees and expense	1,903	3,596	(1,693)	(47.1)%
Stock-based compensation	152	267	(115)	(43.1)%
Other	1,380	1,559	(179)	(11.5)%
Total	<u>\$ 6,460</u>	<u>\$ 8,837</u>	<u>\$ (2,377)</u>	<u>(26.9)%</u>

The change in S&M expense of \$2.4 million for the year ended December 31, 2023 compared to 2022 was primarily due to:

- Personnel and related benefits decreased \$390,000 from \$3.4 million for the year ended December 31, 2022 to \$3.0 million in 2023 due to decreased sales commission and reduced headcount.
- Direct marketing fees and expense decreased \$1.7 million from \$3.6 million for the year ended December 31, 2022 to \$1.9 million in 2023 due to savings associated with the utilization of a more cost-effective patient support services and other Mytesi marketing initiatives.
- Stock-based compensation benefits decreased \$115,000 from \$267,000 for the year ended December 31, 2022 to \$152,000 in 2023 primarily due to lower options and RSUs granted during the period as compared to 2022.
- Other expenses decreased \$179,000 from \$1.6 million for the year ended December 31, 2022 to \$1.4 million 2023 largely due to lower consulting and contractor services but slightly offset by increased travels for sales and marketing personnel.

*General and Administrative Expense*

The following table presents the components of general and administrative ("G&A") expense for the years ended December 31, 2023 and 2022:

(in thousands)	Year Ended December 31,		Variance	Variance %
	2023	2022		
<i>General and Administrative:</i>				
Personnel and related benefits	\$ 5,135	\$ 5,582	\$ (447)	(8.0)%
Legal services	2,009	1,225	784	64.0 %
Public company expense	1,789	2,692	(903)	(33.5)%
Stock-based compensation	916	1,788	(872)	(48.8)%
Lease expense	877	629	248	39.4 %
Third-party consulting services	679	507	172	33.9 %
Audit, tax and accounting services	537	454	83	18.3 %
Travel and other expenses	435	378	57	15.1 %
Other	4,211	4,613	(402)	(8.7)%
<b>Total</b>	<b>\$ 16,588</b>	<b>\$ 17,868</b>	<b>\$ (1,280)</b>	<b>(7.2)%</b>

The change in G&A expenses of \$1.3 million for the year ended December 31, 2023 compared to 2022 was due primarily to:

- Personnel and related benefits decreased \$447,000 from \$5.6 million for the year ended December 31, 2022 to \$5.1 million in 2023 due to lower headcount and no bonus in 2023.
- Legal services increased \$784,000 from \$1.2 million for the year ended December 31, 2022 to \$2.0 million in 2023 primarily due to increased legal consultations for contracts and agreements and other regulatory filings.
- Public company expenses decreased \$903,000 from \$2.7 million for the year ended December 31, 2022 to \$1.8 million in 2023 due to less investor relations and communications consulting expenses, and decreased expenses related to the annual shareholder meetings.
- Stock-based compensation expense decreased \$872,000 from \$1.8 million for the year ended December 31, 2022 to \$916,000 in 2023 primarily due to lower general and administrative expense incurred for options granted with immediate vesting to existing employees.
- Lease expense increased \$248,000 from \$629,000 for the year ended December 31, 2022 to \$877,000 in 2023, primarily due to additional lease space and increase in fees.
- Third-party consulting services increased \$172,000 from \$507,000 for the year ended December 31, 2022 to \$679,000 in 2023, mostly due to the increase in outsourced accounting transactions.
- Audit, tax and accounting services fees increased \$83,000 from \$454,000 for the year ended December 31, 2022 to \$537,000 in 2023, mostly due to the additional financing and complex accounting transactions for the year.
- Other general and administrative expenses decreased \$402,000 from \$4.6 million for the year ended December 31, 2022 to \$4.2 million in 2023 largely due to lower depreciation and amortization of fixed assets and intangible assets, insurance expenses and other support services.

**Impairment Loss on Intangible Asset**

The Company recognized an impairment loss on intangible assets amounting to \$371,000 as a result of impairment evaluation to its internal use software costs – registry triggered by experiencing lower-than-anticipated sales growth for Canalevia and Neonorm, its two primary animal health products.

**Gain or Loss on Extinguishment of Debt**

Gain on extinguishment of debt increased by \$5.9 million from a loss of \$2.2 million for the year ended December 31, 2022 to a gain of \$3.7 million for the same period in 2023 due to significant modifications resulting to extinguishment recognition.

**Change in Fair Value of Freestanding and Hybrid Financial Instruments Designated at FVO**

Change in fair value of freestanding and hybrid financial instruments designated at FVO increased by \$5.1 million from a loss of \$20,000 for the year ended December 31, 2022, to a loss of \$5.1 million for the same period in 2023 primarily due to additional freestanding instruments measured at FVO.

**Interest Expense, net**

Interest expense decreased \$6.3 million from \$12.7 million for the year ended December 31, 2022 to \$6.4 million in 2023 primarily due to the election of certain freestanding instruments to be valued at Fair Value Option ("FVO") upon extinguishment. The lower interest expense was offset by a higher loss in change in fair value of financial instruments and hybrid instrument designated at FVO.

**Liquidity and Capital Resources**

*Sources of Liquidity*

We have incurred net losses since our inception. For the years ended December 31, 2023 and 2022, we had net losses of \$41.9 million and \$48.4 million, respectively, and expect to incur additional losses in the near-term future. At December 31, 2023, we had an accumulated deficit of \$308.2 million and accumulated comprehensive loss of \$652,000. To date, we have generated only limited revenue, and we may never achieve revenue sufficient to offset our expenses.

We had cash of \$6.5 million as of December 31, 2023 to fund our operating plan through one year from the issuance of these consolidated financial statements.

We have funded our operations primarily through the issuance of debt and equity securities, in addition to sales of our commercial products. Cash provided by financing activities for the year ended December 31, 2023, were generated from the issuance of an aggregate of 54,283,779 shares of common stock under the ATM Agreement for total net proceeds of approximately \$32.1 million, issuance of an aggregate 6,850,000 warrants and 137 Series G Convertible Preferred Stock in PIPE financing for a total net proceeds of \$1.8 million, and investment from non-controlling interest for a total net proceeds of \$1.2 million.

We expect our expenditures will continue to increase as we continue our efforts to develop our products and continue the development of our pipeline in the near term. We may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. We may also not be successful in entering into partnerships that include payment of upfront licensing fees for our products and product candidates for markets outside the US, where appropriate. If we do not generate upfront fees from any anticipated arrangements, it would have a negative effect on our operating plan. We still plan to finance our operations and capital funding needs through equity and/or debt financing as well as revenue from future product sales. However, there can be no assurance that additional funding will be available to us on acceptable terms on a

timely basis, if at all, or that we will generate sufficient cash from operations to adequately fund operating needs or ultimately achieve profitability. If we are unable to obtain an adequate level of financing needed for the long-term development and commercialization of our products, we will need to curtail planned activities and reduce costs. Doing so will likely have an adverse effect on our ability to execute on our business plan.

***Cash Flows for Year Ended December 31, 2023 compared to the Year Ended December 31, 2022***

The following table shows a summary of cash flows for the years ended December 31, 2023 and 2022:

(in thousands)	<b>Year Ended December 31,</b>	
	<b>2023</b>	<b>2022</b>
Total cash used in operating activities	\$ (33,242)	\$ (33,104)
Total cash used in investing activities	—	(1,675)
Total cash provided by financing activities	34,227	23,181
Effects of foreign exchange rate changes on assets and liabilities	15	16
<b>Net increase (decrease) in cash</b>	<b>\$ 1,000</b>	<b>\$ (11,582)</b>

***Cash Used in Operating Activities***

During the year ended December 31, 2023, net cash used in operating activities of \$33.2 million resulted from our net comprehensive loss of \$41.9 million adjusted by amortization of debt issuance costs, debt discount, and non-cash interest expense of \$13.2 million, Change in fair value of freestanding and hybrid financial instruments designated at FVO of \$5.1 million, stock-based compensation of \$2.1 million, depreciation and amortization expenses of \$2.0 million, amortization of operating lease right-of-use assets of \$375,000, impairment loss on intangible asset of \$371,000, shares issued in exchange for services of \$171,000, share in joint venture's loss of \$51,000, gain on extinguishment of debt \$3.7 million, and net changes in operating assets and liabilities of \$11.1 million.

During the year ended December 31, 2022, net cash used in operating activities of \$33.1 million resulted from our net comprehensive loss of \$49.1 million adjusted by amortization of debt issuance costs, debt discount, and non-cash interest expense of \$11.8 million, stock-based compensation of \$3.3 million, loss on extinguishment of debt of \$2.2 million, depreciation and amortization expenses of \$2.0 million, shares issued in exchange for services of \$823,000, amortization of operating lease right-of-use assets of \$311,000, change in fair value of hybrid instruments designated at FVO of \$21,000, and net changes in operating assets and liabilities of \$4.4 million.

***Cash Used in Investing Activities***

There are no cash used in investing activities during the year ended December 31, 2023.

During the year ended December 31, 2022, cash used in investing activities was \$1.7 million which consisted of cash used in software development activities of \$1.6 million and cash used to purchase property and equipment of \$77,000.

***Cash Provided by Financing Activities***

During the year ended December 31, 2023, net cash provided by financing activities of \$34.2 million consisted of \$32.1 million in net proceeds from shares issued in an At the Market offering, \$1.2 million net proceeds from issuance of warrants in PIPE financing, investment from non-controlling interest of \$1.2 million and \$611,000 net proceeds from issuance of preferred shares in PIPE financing, offset by \$853,000 repayment of insurance financing, and \$100,000 in principal payments of Tempesta Note.

During the year ended December 31, 2022, net cash provided by financing activities of \$23.2 million consisted of \$20.5 million in net proceeds from shares issued in an At the Market offering, \$4.0 million in net proceeds from notes payable with Streeterville, offset by \$1.2 million repayment of insurance financing and \$100,000 payment of Tempesta Note.

**ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK.**

Not applicable.

**ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA**

**Jaguar Health, Inc.  
Index to Financial Statements**

	<u>Page</u>
<b>Financial Statements</b>	
<a href="#">Reports of Independent Registered Public Accounting Firms</a>	84
<a href="#">Consolidated Balance Sheets as of December 31, 2023 and 2022</a>	86
<a href="#">Consolidated Statements of Operations for the years ended December 31, 2023 and 2022</a>	87
<a href="#">Consolidated Statements of Comprehensive Loss for the years ended December 31, 2023 and 2022</a>	88
<a href="#">Consolidated Statements of Changes in Stockholders' Equity for the years ended December 31, 2023 and 2022</a>	89
<a href="#">Consolidated Statements of Cash Flows for the years ended December 31, 2023 and 2022</a>	91
<a href="#">Notes to Consolidated Financial Statements</a>	93



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**Report of Independent Registered Public Accounting Firm**

To the Board of Directors and  
Stockholders of Jaguar Health, Inc.:

**Opinion on the Financial Statements**

We have audited the accompanying consolidated balance sheets of Jaguar Health, Inc., and subsidiaries (the "Company") as of December 31, 2023 and 2022, and the related consolidated statements of operations, comprehensive loss, changes in stockholders' equity, and cash flows for each of the years in the two-year period ended December 31, 2023, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2023, and 2022 and the results of its operations and its cash flows for each of the years in the two-year period ended December 31, 2023, in conformity with accounting principles generally accepted in the United States of America.

**The Company's Ability to Continue as a Going Concern**

The accompanying consolidated financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the consolidated financial statements, the Company has an accumulated deficit, recurring losses, and expects continuing future losses. These conditions raise substantial doubt about the Company's ability to continue as a going concern. Management's evaluation of the events and conditions and management's plans regarding these matters are also described in Note 1. The consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty.

**Basis for Opinion**

These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audit.

We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audit, we are required to obtain an understanding of internal control over financial reporting, but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

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Our audit included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audit provides a reasonable basis for our opinion.

**Critical Audit Matters**

The critical audit matter communicated below is a matter arising from the current period audit of the consolidated financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the consolidated financial statements and (2) involved our especially challenging, subjective, or complex judgments. We determined that there are no critical audit matters.

/s/ RBSM, LLP

**RBSM LLP**

We have served as the Company's auditor since 2022.  
Larkspur, California  
April 1, 2024

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**JAGUAR HEALTH, INC.**  
**CONSOLIDATED BALANCE SHEETS**

(In thousands, except share and per share data)	<b>December 31, 2023</b>	<b>December 31, 2022</b>
<b>Assets</b>		
Current assets:		
Cash	\$ 6,469	\$ 5,469
Accounts receivable, net	1,967	1,879
Other receivable	217	588
Inventory	9,189	7,024
Prepaid expenses and other current assets	<u>10,121</u>	<u>7,361</u>
Total current assets	27,963	22,321
Property and equipment, net	496	557
Operating lease - right-of-use asset	1,176	1,140
Intangible assets, net	20,116	22,439
Other assets	1,012	995
<b>Total assets</b>	<b>\$ 50,763</b>	<b>\$ 47,452</b>
<b>Liabilities and Stockholders' equity (deficit)</b>		
Current liabilities:		
Accounts payable	\$ 4,974	\$ 5,808
Accrued liabilities	3,798	8,165
Operating lease liability, current	348	483
Notes payable, current	4,867	15,883
Total current liabilities	13,987	30,339
Operating lease liability, net of current portion	886	725
Notes payable, net of discount, net of current portion (includes notes designated at Fair Value Option amounting to \$ 31.0 million as of December 31, 2023 and \$ 7.8 million December 31, 2022, respectively)	30,993	17,744
Total liabilities	<b>45,866</b>	<b>48,808</b>
Commitments and contingencies (See Note 5)		
<b>Stockholders' equity (deficit)</b>		
Series G convertible preferred stock: \$ 0.0001 par value; 137 and zero shares designated from 10,000,000 preferred stock authorized at December 31, 2023 and December 31, 2022; 122 and zero shares issued and outstanding at December 31, 2023 and December 31, 2022	—	—
Series H convertible preferred stock: \$ 0.0001 par value; 105 and zero shares designated from 10,000,000 preferred stock authorized at December 31, 2023 and December 31, 2022; zero shares issued and outstanding at December 31, 2023 and December 31, 2022	—	—
Series I convertible preferred stock: \$ 0.0001 par value; 118 and zero shares designated from 10,000,000 preferred stock authorized at December 31, 2023 and December 31, 2022; 56 and zero shares issued and outstanding at December 31, 2023 and December 31, 2022	—	—
Common stock - voting: \$ 0.0001 par value, 298,000,000 shares authorized at December 31, 2023 and December 31, 2022; 73,413,248 and 2,182,084 issued and outstanding at December 31, 2023 and December 31, 2022	7	—
Common stock - non-voting: \$ 0.0001 par value, 50,000,000 shares authorized at December 31, 2023 and December 31, 2022; 9 shares issued and outstanding at December 31, 2023 and December 31, 2022	—	—
Additional paid-in capital	313,854	266,971
Noncontrolling interest	( 64 )	( 699 )
Accumulated deficit	( 308,248 )	( 266,948 )
Accumulated other comprehensive loss	( 652 )	( 680 )
Total stockholders' equity (deficit)	4,897	( 1,356 )
<b>Total liabilities and stockholders' equity (deficit)</b>	<b>\$ 50,763</b>	<b>\$ 47,452</b>

The accompanying notes are an integral part of these consolidated financial statements.

**JAGUAR HEALTH, INC.**  
**CONSOLIDATED STATEMENTS OF OPERATIONS**

(In thousands, except share and per share data)	Year Ended December 31,	
	2023	2022
Product revenue, net	\$ 9,761	\$ 11,956
Operating expenses		
Cost of product revenue	2,037	2,019
Research and development	18,596	17,647
Sales and marketing	6,460	8,837
General and administrative	16,588	17,868
Impairment loss on intangible assets	371	—
Total operating expenses	44,052	46,371
Loss from operations	( 34,291 )	( 34,415 )
Interest expense	( 6,382 )	( 12,723 )
Change in fair value of freestanding and hybrid financial instruments designated at		
Fair Value Option	( 5,125 )	( 20 )
Gain (loss) on extinguishment of debt	3,697	( 2,187 )
Other income	200	950
Loss before income tax	( 41,901 )	( 48,395 )
Income tax expense	—	—
Net loss	( 41,901 )	( 48,395 )
Net loss attributable to noncontrolling interest	\$ ( 601 )	\$ ( 941 )
Net loss attributable to common stockholders	\$ ( 41,300 )	\$ ( 47,454 )
Net loss per share, basic	\$ ( 1.79 )	\$ ( 36.18 )
Net loss per share, diluted	\$ ( 1.79 )	\$ ( 36.18 )
Weighted-average common stock outstanding, basic	23,068,423	1,311,519
Weighted-average common stock outstanding, diluted	23,068,423	1,311,519

The accompanying notes are an integral part of these consolidated financial statements.

**JAGUAR HEALTH, INC.**  
**CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS**

	<b>Year Ended December 31,</b>	
(In thousands, except share and per share data)	<b>2023</b>	<b>2022</b>
Net loss	\$ (41,901)	\$ (48,395)
Other comprehensive income (loss)	31	(680)
Net comprehensive loss	<u>\$ (41,870)</u>	<u>\$ (49,075)</u>
<b>Common stockholders:</b>		
Net loss attributable to common stockholders	\$ (41,300)	\$ (47,454)
Other comprehensive loss attributable to common stockholders	28	(680)
Net comprehensive loss attributable to common stockholders	<u>\$ (41,272)</u>	<u>\$ (48,134)</u>
<b>Non-controlling interests:</b>		
Net loss attributable to non-controlling interests	\$ (601)	\$ (941)
Other comprehensive loss attributable to non-controlling interests	3	—
Net comprehensive loss attributable to non-controlling interests	<u>\$ (598)</u>	<u>\$ (941)</u>

The accompanying notes are an integral part of these consolidated financial statements.

**JAGUAR HEALTH, INC.**  
**CONSOLIDATED STATEMENTS OF CHANGES IN STOCKHOLDERS' EQUITY (DEFICIT)**

(In thousands, except share data)	Series G Convertible preferred stock	Series H Convertible preferred stock	Series I Convertible preferred stock	Common Stock - voting	Common Stock - non- voting	Additional	Noncontrolling	Accumulated other compre- hensive	Total Stockholders			
	Shares	Amount	Shares	Amount	Shares	Amount	paid-in capital	interest	deficit	loss	(Deficit)	
<b>Balances as of January 1, 2022</b>	—	\$ —	—	\$ —	—	\$ 644,700	\$ —	9 \$ —	\$ 231,105	\$ 242	\$ (219,494) \$ —	\$ 11,853
Common stock issued in At the Market offering, net of issuance and offering costs of \$ 103	—	—	—	—	—	923,164	—	—	20,462	—	—	20,462
Common stock issued to Iliad in exchange of notes payable and accrued interest	—	—	—	—	—	235,461	—	—	6,207	—	—	6,207
Common stock issued to Streeterville in exchange of notes payable and accrued interest	—	—	—	—	—	310,196	—	—	5,056	—	—	5,056
Shares issued to Synworld for services	—	—	—	—	—	45,896	—	—	800	—	—	800
Common stock issued upon exercise of restricted stock units	—	—	—	—	—	2,516	—	—	100	—	—	100
Common stock issued to other third party for services	—	—	—	—	—	20,151	—	—	23	—	—	23
Stock-based compensation	—	—	—	—	—	—	—	—	3,218	—	—	3,218
Net loss	—	—	—	—	—	—	—	—	(941)	(47,454)	—	(48,395)
Translation loss	—	—	—	—	—	—	—	—	—	—	(680)	(680)
<b>Balances as of December 31, 2022</b>	<b>—</b>	<b>\$ —</b>	<b>—</b>	<b>\$ —</b>	<b>—</b>	<b>\$ 2,182,084</b>	<b>\$ —</b>	<b>9 \$ —</b>	<b>\$ 266,971</b>	<b>\$ (699)</b>	<b>\$ (266,948)</b>	<b>\$ (680) \$ (1,356)</b>

The accompanying notes are an integral part of these consolidated financial statements.

[Table of Contents](#)

(In thousands, except share data)	Series G Convertible preferred stock	Series H Convertible preferred stock	Series I Convertible preferred stock	Common Stock - voting	Common Stock - non- voting	Additional	Noncontrolling	Accumulated other comprehensive	Accumulated loss	Total Stockholders' Equity
	Shares	Amount	Shares	Amount	Shares	Amount	paid-in capital	interest	deficit	(680) \$ (1,356)
<b>Balances as of January 1, 2023</b>	—	—	—	2,182,084	\$ —	9	\$ —	266,971	\$ (699)	\$ (266,948)
Common stock issued in At the Market offering, net of issuance and offering costs of \$ 242	—	—	—	54,283,779	6	—	—	32,094	—	—
Preferred stock issued in PIPE financing, net of issuance and offering costs of \$ 12	137	—	—	—	—	—	—	611	—	611
Preferred stock issued to Streeterville in exchange of notes payable and accrued interest	—	—	73	—	—	—	—	1,730	—	—
Preferred stock issued to Irving in exchange of notes payable and accrued interest	—	—	32	—	118	—	—	2,201	—	2,201
Common stock issued to Iliad in exchange of notes payable and accrued interest	—	—	—	—	6,245,005	1	—	2,063	—	2,064
Common shares issued to Streeterville from conversion of Series H Preferred Stock	—	—	(73)	—	—	3,650,000	—	—	—	—
Common shares issued to Irving from conversion of Series I Preferred Stock	—	—	—	(62)	—	2,985,362	—	—	—	—
Common stock issued to Irving in exchange of notes payable and accrued interest	—	—	—	—	2,058,651	—	—	2,022	—	2,022
Common shares issued to Irving from conversion of Series H Preferred Stock	—	—	(32)	—	—	1,600,000	—	—	—	—
Common shares issued to from conversion of Series G Preferred Stock	(15)	—	—	—	375,000	—	—	—	—	—
Common stock issued upon exercise of restricted stock units	—	—	—	—	13,149	—	—	9	—	9
Common stock issued to other third party for services	—	—	—	—	18,869	—	—	171	—	171
RSUs issued	—	—	—	—	1,349	—	—	—	—	—
Warrants issued to Irving in exchange of Standstill Warrants issued in PIPE financing	—	—	—	—	—	—	—	1,934	—	1,934
Warrants issued to Iliad in exchange of Standstill Warrants issued to Irving through Royal Global Amendment Exchange	—	—	—	—	—	—	—	1,236	—	1,236
Warrants issued to Irving through Royal Global Amendment Exchange	—	—	—	—	—	—	—	535	—	535
Warrants issued to Streeterville through Royal Global Amendment Exchange	—	—	—	—	—	—	—	61	—	61
Warrants issued to Iliad through Royal Global Amendment Exchange	—	—	—	—	—	—	—	59	—	59
Stock-based compensation	—	—	—	—	—	—	—	54	—	54
Additional investment from non-controlling interests	—	—	—	—	—	—	—	2,103	—	2,103
Net loss	—	—	—	—	—	—	—	—	1,233	—
Translation gain	—	—	—	—	—	—	—	(601)	(41,300)	(41,901)
<b>Balances as of December 31, 2023</b>	<b>122</b>	<b>\$ —</b>	<b>56</b>	<b>\$ 73,413,248</b>	<b>\$ 7</b>	<b>9</b>	<b>\$ 313,854</b>	<b>\$ (64)</b>	<b>\$ (308,248)</b>	<b>\$ (652) \$ 4,897</b>

The accompanying notes are an integral part of these consolidated financial statements

**JAGUAR HEALTH, INC.**  
**CONSOLIDATED STATEMENTS OF CASH FLOWS**

	Year Ended December 31,	
	2023	2022
(in thousands)		
<b>Cash flows from operating activities</b>		
Net comprehensive loss	\$ ( 41,870 )	\$ ( 49,075 )
Adjustments to reconcile net loss and comprehensive loss to net cash used in operating activities:		
Amortization of debt issuance costs, debt discount, and non-cash interest expense	13,206	11,758
Change in fair value of freestanding and hybrid financial instruments designated at Fair Value Option	5,125	21
Stock-based compensation, vested and released restricted stock units and exercised stock options	2,112	3,318
Depreciation and amortization expenses	2,013	1,981
Amortization of operating lease - right-of-use-asset	375	311
Impairment loss on intangible assets	371	—
Shares issued in exchange for services	171	823
Share in joint venture's loss	51	—
(Gain) Loss on extinguishment of debt	( 3,697 )	2,187
Changes in assets and liabilities		
Accounts receivable	( 88 )	( 170 )
Other receivable	386	( 251 )
Inventory	( 2,165 )	( 2,124 )
Prepaid expenses and other current assets	( 5,011 )	( 1,560 )
Other assets	( 17 )	( 550 )
Accounts payable	( 855 )	902
Accrued liabilities	( 2,955 )	( 360 )
Operating lease liability	( 394 )	( 315 )
Total cash used in operating activities	<u>( 33,242 )</u>	<u>( 33,104 )</u>
<b>Cash flows from investing activities</b>		
Purchase of equipment	—	( 77 )
Purchase of intangible assets	—	( 1,598 )
Total cash used in investing activities	<u>—</u>	<u>( 1,675 )</u>
<b>Cash flows from financing activities</b>		
Proceeds from issuance of shares in At the Market offering, net of issuance and offering costs of \$242 and \$ 103 in 2023 and 2022, respectively	32,100	20,462
Proceeds from issuance of warrants in PIPE financing	1,236	—
Investment from non-controlling interest	1,233	—
Proceeds from issuance of preferred stock in PIPE financing, net of issuance cost of \$12	611	—
Payment of Tempesta Note	( 100 )	( 100 )
Repayment of insurance financing	( 853 )	( 1,156 )
Proceeds from notes payable with Streeterville	—	3,975
Total cash provided by financing activities	<u>34,227</u>	<u>23,181</u>
Effects of foreign exchange rate changes on assets and liabilities	15	16
<b>Net increase (decrease) in cash</b>	<u>1,000</u>	<u>( 11,582 )</u>
<b>Cash at beginning of the year</b>	<u>5,469</u>	<u>17,051</u>
<b>Cash at end of the year</b>	<u><u>\$ 6,469</u></u>	<u><u>\$ 5,469</u></u>

**JAGUAR HEALTH, INC.**  
**STATEMENTS OF CASH FLOWS (continued)**

	Year Ended December 31,	
	2023	2022
<b>Supplemental schedule of cash flow information</b>		
Cash paid for interest	\$ 35	\$ 23
<b>Supplemental schedule of non-cash financing and investing activities</b>		
Preferred stock issued to Irving in exchange of notes payable and accrued interest	\$ 2,201	\$ —
Common stock issued to Irving in exchange of notes payable and accrued interest	\$ 2,022	\$ —
Warrants issued to Irving in exchange of Standstill	\$ 1,934	\$ —
Preferred stock issued to Streeterville in exchange of notes payable and accrued interest	\$ 1,730	\$ 792
Common stock issued to Iliad in exchange of notes payable and accrued interest	\$ 2,064	\$ 10,472
First Insurance Financing	\$ 676	\$ 1,056
Warrants issued to Iliad in exchange of Standstill	\$ 535	\$ —
Lease modification	\$ 441	\$ —
Umbrella Insurance Financing	\$ 110	\$ —
Warrants issued to Irving due to Royal Interest Global Amendment	\$ 61	\$ —
Warrants issued to Streeterville due to Royal Interest Global Amendment	\$ 59	\$ —
Warrants issued to Iliad due to Royal Interest Global Amendment	\$ 54	\$ —
Recognition of operating lease - right-of-use asset and operating lease liability	<u>\$ 30</u>	<u>\$ 365</u>

The accompanying notes are an integral part of these consolidated financial statements.

**Jaguar Health, Inc.  
Notes to Consolidated Financial Statements**

**1. Organization and Business**

Jaguar Health, Inc. ("Jaguar" or the "Company") was founded in San Francisco, California as a Delaware corporation on June 6, 2013 (inception). The Company was a majority-owned subsidiary of Napo Pharmaceuticals ("Napo") until the close of the Company's initial public offering on May 18, 2015. The Company was formed to develop and commercialize first-in-class prescription and non-prescription products for companion animals.

On July 31, 2017, Jaguar completed a merger with Napo pursuant to the Agreement and Plan of Merger dated March 31, 2017, by and among Jaguar, Napo, Napo Acquisition Corporation ("Merger Sub"), and Napo's representative (the "Merger Agreement"). In accordance with the terms of the Merger Agreement, upon the completion of the merger, Merger Sub merged with and into Napo, with Napo surviving as the wholly owned subsidiary (the "Merger" or "Napo Merger"). Immediately following the Merger, Jaguar changed its name from "Jaguar Animal Health, Inc." to "Jaguar Health, Inc." Napo now operates as a wholly owned subsidiary of Jaguar focused on human health including the ongoing development of crofelemer and commercialization of Mytesi.

On March 15, 2021, Jaguar established Napo EU S.p.A (which changed its name in December 2021 to "Napo Therapeutics") in Milan, Italy as a subsidiary of Napo. Napo Therapeutics' core mission is to provide access to crofelemer in Europe to address significant rare/orphan disease indications, including, initially, two key orphan target indications: Short bowel syndrome ("SBS") with intestinal failure and congenital diarrheal disorders ("CDD").

The Company manages its operations through two segments – human health and animal health and is headquartered in San Francisco, California.

***Nasdaq Communication and Compliance***

***Minimum Stockholders' Equity Requirement***

On May 10, 2023, the Company received a letter from the Staff of Nasdaq indicating that the bid price for the Company's common stock for the last 30 consecutive business days had closed below the minimum \$ 1.00 per share required for continued listing under Nasdaq Listing Rule 5550(a)(2).

Under Nasdaq Listing Rule 5810(c)(3)(A), the Company has been granted a 180 -calendar day grace period, or until November 6, 2023, to regain compliance with the minimum bid price requirement. The continued listing standard will be met if the Company evidences a closing bid price of at least \$ 1.00 per share for a minimum of 10 consecutive business days during the 180 calendar-day grace period. In order for Nasdaq to consider granting the Company additional time beyond November 6, 2023, the Company would be required, among other things, to meet the continued listing requirement for the market value of publicly held shares as well as all other standards for initial listing on Nasdaq, with the exception of the minimum bid price requirement. If measured today, the Company would qualify for Nasdaq's consideration of an extension because the Company currently has stockholders' equity of at least \$ 2.5 million. In the event the Company does not regain compliance with the \$ 1.00 bid price requirement by November 6, 2023, eligibility for Nasdaq's consideration of a second 180 -day day grace period would be determined on the Company's compliance with the above referenced criteria on November 6, 2023.

On November 8, 2023, the Company received a formal notice from the Staff of Nasdaq granting the Company an additional 180-day grace period, through May 6, 2024 to regain compliance with the \$ 1.00 bid price requirement for the continued listing on the Nasdaq Capital Market.

### **Liquidity and Going Concern**

The Company, since its inception, has incurred recurring operating losses and negative cash flows from operations and has an accumulated deficit of \$ 308.2 million as of December 31, 2023. The Company expects to incur substantial losses and negative cash flows in future periods. Further, the Company's future operations, which include the satisfaction of current obligations, are dependent on the success of the Company's ongoing development and commercialization efforts, as well as securing of additional financing and generating positive cash flows from operations. There is no assurance that the Company will have adequate cash balances to maintain its operations.

Although the Company plans to finance its operations and cash flow needs through equity and/or debt financing, collaboration arrangements with other entities, license royalty agreements, joint ventures, as well as revenue from future product sales, the Company does not believe its current cash balances are sufficient to fund its operating plan through one year from the issuance of these consolidated financial statements. There can be no assurance that additional funding will be available to the Company on acceptable terms, or on a timely basis, if at all, or that the Company will generate sufficient cash from operations to adequately fund operating needs. If the Company is unable to obtain an adequate level of financing needed for the long-term development and commercialization of our products, the Company will need to curtail planned activities and reduce costs. Doing so will likely have an adverse effect on the ability to execute the Company's business plan; accordingly, there is substantial doubt about the ability of the Company to continue in existence as a going concern. The accompanying audited consolidated financial statements do not include any adjustments that might result from the outcome of these uncertainties.

## **2. Summary of Significant Accounting Policies**

### ***Basis of Presentation***

The audited consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America ("US GAAP").

### ***Principles of Consolidation***

The consolidated financial statements have been prepared in accordance with US GAAP and applicable rules and regulations of the Securities and Exchange Commission ("SEC") and include the accounts of the Company and its subsidiaries. All inter-company transactions and balances have been eliminated in consolidation. The reporting currency of the Company is the US dollar.

### ***Non-controlling interest***

The Company consolidates the results of Napo Therapeutics, which was owned 88 % and 90 % by the Company and 12 % and 10 % by private investors as of December 31, 2023 and 2022, respectively. The potential voting rights with a certainty of being exercised in its shares are included in the ownership percentage. During the year ended December 31, 2023, an additional investment from a private entity amounting to € 1.1 million equivalent to \$ 1.23 million resulted in the increase in non-controlling interest percentage.

### ***Use of Estimates***

The preparation of the consolidated financial statements in conformity with US GAAP requires the Company's management to make judgments, assumptions and estimates that affect the amounts reported in its audited consolidated financial statements and the accompanying notes. The accounting policies that reflect the Company's more significant estimates and judgments and that the Company believes are the most critical to aid in fully understanding and evaluating its reported financial results are the valuation of stock options, restricted stock units ("RSUs"), valuation of freestanding and hybrid instruments designated at fair value option ("FVO"), valuation of warrant liabilities, acquired in-process research and development ("IPR&D"), and useful lives assigned to long-lived

assets; impairment assessment of non-financial assets; valuation adjustments for excess and obsolete inventory; allowance for doubtful accounts; deferred taxes and valuation allowances on deferred tax assets; evaluation and measurement of contingencies; and recognition of revenue, including estimates for product returns. Those estimates could change, and as a result, actual results could differ materially from those estimates.

#### **Cash**

The Company's cash on deposit may exceed the US and European federally insured limits at certain times during the year. The Company maintains cash accounts with certain major financial institutions in the US and Europe. The Company does not have cash equivalents as of December 31, 2023 and 2022.

#### **Accounts Receivable**

Accounts receivable is recorded net of allowances for discounts for prompt payment and credit losses.

The Company utilizes a loss rate approach in determining its lifetime expected credit losses on receivables from customers. This method calculates an estimate of credit losses based on historical experience, credit quality, age of the accounts receivable balances, and current and forecasted economic and business conditions that may affect a customer's ability to pay. In determining the loss rates, the Company evaluates information related to its historical losses, adjusted for existing conditions and further adjusted for the period of time that can reasonably be forecasted. The facts and circumstances as of the balance sheet date are used to adjust the estimate for periods beyond those that can reasonably be forecasted.

The past due status of accounts receivable is determined based on the contractual due dates for payments. Receivable is deemed past due when payment hasn't been received 30 days after the contractual due date. The credit loss allowance was immaterial as of December 31, 2023 and 2022. The corresponding expense for the credit loss allowance is reflected in general and administrative expenses.

#### **Current Expected Credit Losses**

The Company recognizes an allowance for credit losses for financial assets carried at amortized cost to present the net amount expected to be collected as of the balance sheet date. Such allowance is based on credit losses that are expected to arise over the contractual term of the asset, which includes consideration of historical credit loss information adjusted for current conditions and reasonable and supportable forecasts.

Changes in the allowance for credit losses are recorded as provision of (or reversal of) credit loss expense. Assets are written off when the Company determines that such are deemed uncollectible. Write-offs are recognized as a deduction from the allowance for credit losses. Expected recoveries of amounts previously written off, not to exceed the aggregate of the amount previously written off, are included in determining the necessary allowance at the balance sheet date.

#### **Concentrations**

Cash is the financial instrument that potentially subjects the Company to a concentration of credit risk as cash is deposited with banks and cash balances are generally in excess of Federal Deposit Insurance Corporation ("FDIC") insurance limits.

For the years ended December 31, 2023 and 2022, substantially all of the Company's revenue was derived from the sale of Mytesi. In looking at sales by the Company to distributors whose net revenue percentage of total net revenue was equal to or greater than 10 %, for fiscal years 2023 and 2022, the Company earned Mytesi revenue

primarily from two major pharmaceutical distributor(s) located in the US, respectively. Revenue earned from each major customer as a percentage of total revenue is as follows:

	Year Ended December 31,	
	2023	2022
Customer 1	28 %	35 %
Customer 2	56 %	53 %

The Company is subject to credit risk from its accounts receivable related to its sales. The Company generally does not perform evaluations of customers' financial condition and generally does not require collateral. Accounts receivable balance of the significant customers as a percentage of total accounts receivable is as follows:

	December 31, 2023	December 31, 2022
Customer 1	32 %	38 %
Customer 2	57 %	54 %

The Company is subject to concentration risk from its suppliers. The Company sources raw material used to produce the active pharmaceutical ingredient ("API") in Mytesi from two suppliers and is dependent on a single third-party contract as well for the supply of finished products for commercialization.

#### ***Other Risks and Uncertainties***

The Company's future results of operations involve a number of risks and uncertainties. Factors that could affect the Company's future operating results and cause actual results to vary materially from expectations including, but not limited to, war, rapid technological change, obtaining second source suppliers and manufacturers, regulatory approval from the US Food and Drug Administration ("FDA") or other regulatory authorities, the results of clinical trials and the achievement of milestones, market acceptance of the Company's product candidates, competition from other products and larger companies, protection of proprietary technology, strategic relationships and dependence on key individuals.

#### *Other Global Events*

Macroeconomic conditions around the world are subject to constant change, influenced by several factors, including persistently high inflation, structural weaknesses in the labor market, low productivity growth, and adverse weather conditions. The UK's recession has severely impacted Europe's decline. The Company's subsidiary in Italy, Napo Therapeutics, has not generated any revenue for the year ending December 31, 2023. Despite these recent global events, there have been no significant changes in the subsidiary's operations.

#### ***Fair Value***

The Company's financial instruments include accounts receivable, net, other receivable, accounts payable, accrued liabilities, operating lease liability and debt. The recorded carrying amount of accounts receivable, accounts payable and accrued liabilities reflect their fair value due to their short-term nature. Other financial liabilities are initially recorded at fair value, and subsequently measured at either fair value or amortized cost using the effective interest method. See Note 3 for the fair value measurements.

**Fair Value Option**

ASC 825-10, *Financial Instruments*, provides FVO election that allows companies an irrevocable election to use fair value as the initial and subsequent accounting measurement attribute for certain financial assets and liabilities. ASC 825-10 permits entities to elect to measure eligible financial assets and liabilities at fair value on an ongoing basis. Unrealized gains and losses on items for which the FVO has been elected are reported in earnings. The decision to elect the FVO is determined on an instrument-by-instrument basis, must be applied to an entire instrument and is irrevocable once elected. Assets and liabilities measured at fair value pursuant to ASC 825-10 are required to be reported separately from those instruments measured using another accounting method. In accordance with the options presented in ASC 825-10, the Company elected to present the aggregate of fair value and non-fair-value amounts in the same line item in the consolidated balance sheets and parenthetically disclose the amount measured at fair value in the aggregate amount. The fair values of the Company's financial instruments reflect the amounts that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date (exit price). The fair value estimates presented in these financial statements are based on information available to the Company as of December 31, 2023 and 2022.

**Inventory**

Inventory is stated at the lower of cost or net realizable value. Cost is determined using the first-in, first-out method. Cost is initially recorded at the invoiced amount of raw materials or API, including the sum of qualified expenditures and charges in bringing the inventory to its existing condition and location. The Company calculates inventory valuation adjustments when conditions indicate that net realizable value is less than cost due to physical deterioration, usage, obsolescence, reductions in estimated future demand or reduction in selling price. Inventory write-downs are measured as the difference between the cost of inventory and net realizable value. The Company does not have an allowance for inventory obsolescence as of December 31, 2023 and 2022.

**Prelaunch Inventory**

The Company's policy is to capitalize costs for prelaunch inventories within the drug development phase that evidence that the product's reasonably likely critical attributes for success are present and feasible, and the key causes of failures are absent based on management's assumptions. The costs that can be capitalized for pre-launch inventory are recorded as "Prepayments and Other Assets".

**Property and Equipment**

Land is stated at cost, reflecting fair value of the property at July 31, 2017, the date of the Napo merger. Equipment is stated at cost, net of accumulated depreciation. Equipment begins to be depreciated when it is placed into service. Depreciation is calculated using the straight-line method over estimated useful lives ranging between 3 to 10 years.

Expenditures for repairs and maintenance of assets are charged to expense as incurred. Costs of major additions and betterments are capitalized and depreciated on a straight-line basis over their estimated useful lives. Upon retirement or sale, the cost and related accumulated depreciation of assets disposed of are removed from the accounts and any resulting gain or loss is included in the audited consolidated comprehensive loss.

**Software Developed for Internal Use**

The Company capitalizes the costs of developing software for internal use. These costs include both purchased software and internally developed software. Costs of developing software are expensed until technological feasibility has been established. Thereafter, all costs are capitalized and are carried at the lower of unamortized cost or net realizable value. Internally developed and purchased software costs are generally amortized over five years.

### **Long-Lived Assets**

The Company regularly reviews the carrying value and estimated lives of all of its long-lived assets, including property and equipment and definite-lived intangible assets, to determine whether indicators of impairment exist that warrant adjustments to carrying values or estimated useful lives. The determinants used for this evaluation include management's estimate of the asset's ability to generate positive income from operations and positive cash flow in future periods as well as the strategic significance of the assets to the Company's business objectives. If the Company determines that events or changes in circumstances indicate that the carrying amount of the asset group may not be recoverable, the Company evaluates the realizability of its long-lived assets (asset group) based on a comparison of projected undiscounted cash flows from use and eventual disposition with the carrying value of the related asset. Any write-downs (which are measured based on the difference between the fair value and the carrying value of the asset) are treated as permanent reductions in the carrying amount of the assets (asset group).

The Company evaluated the carrying value of its internal use software costs as at December 31, 2023 in accordance with ASC 360-10, *Impairment of Long-lived Assets to be Held or Used*. Based on the evaluation, the Company determined that the internal use software costs – registry's carrying value as of December 31, 2023, were no longer recoverable and recorded a corresponding impairment loss. The impairment loss was calculated as the difference between the registry's carrying value and its estimated fair value on December 31, 2023. The fair value was determined using a discounted cash flow ("DCF") model, a Level 3 evaluation technique under ASC 820, *Fair Value Measurements*. The DCF model utilized entity-specific assumptions regarding future sales volume, pricing and costs. These assumptions considered factors such as continuity of existing customer relationships, potential shifts in economic conditions and other relevant market influences. The net cash flows generated by the model were then discounted to present value using a rate reflective of the time value of money and the inherent use associated with the expected cash flows. The discount rate was based on the comparable debt instrument deemed appropriate by management. Given the changing market conditions, there is a reasonable possibility that the estimates used to determine the registry's fair value may require adjustments in the near future. Any such changes in assumptions could result in further impairment charges. The Company recognized an expense for the year ended December 31, 2023, and a corresponding reduction in the carrying value of the internal use software-registry as a result of the impairment.

As at December 31, 2022, none of the Company's long-lived assets were deemed impaired.

### **Indefinite-lived Intangible Assets**

Acquired IPR&D are intangible assets acquired in the July 2017 Napo merger. Under ASC 805, *Business Combinations*, IPR&D are initially recognized at fair value and classified as indefinite-lived assets until the successful completion or abandonment of the associated research and development efforts. During the development period, these assets will not be amortized as charges to earnings; instead, these assets will be tested for impairment on an annual basis or more frequently if impairment indicators are identified. An impairment loss is measured based on the excess of the carrying amount over the asset's fair value. The Company had no impairment of indefinite-lived intangible assets for the years ended December 31, 2023 and 2022.

### **Leases**

The Company accounts for its leases in accordance with ASC 842, *Leases*.

At the inception of an arrangement, the Company determines whether the arrangement is or contains a lease based on the unique facts and circumstances present. Operating lease liabilities and their corresponding right-of-use assets are recorded based on the present value of lease payments over the expected lease term. Because the interest rate implicit in lease contracts is typically not readily determinable, the Company utilizes its incremental borrowing rate, which is the rate incurred to borrow on a collateralized basis over a similar term, an amount equal to the lease payments in a similar economic environment. Certain adjustments to the right-of-use asset may be required for items such as initial direct costs paid or incentives received.

The Company elected to include both the lease and non-lease components as a single component and account for it as a lease.

**Lease Modification**

ASC 842 defines lease modification as a change to the terms and conditions of a contract that results in a change in the scope of or the consideration for a lease. A lease modification can result in either a separate new contract that is accounted for separately from the original contract or a single modified contract.

The Company shall account for a modification to a contract as a separate contract when the modification grants the lessee an additional right of use not included in the original lease and the lease payments increase commensurate with the standalone price for the additional right of use, adjusted for the circumstances of the particular contract. When the Company concludes that a lease modification should be accounted for as a new contract that is separate and apart from the original lease, the new contract should be evaluated for whether it is a lease or contains an embedded lease. If the new contract is a lease or contains an embedded lease, the new lease should be accounted for as any other new lease. The new lease is recorded on the commencement date of the new lease, which is the date the lessee has access to the leased asset.

If a lease modification is not accounted for as a separate contract, the Company should reassess whether the contract contains a lease. If the modified contract is a lease or contains an embedded lease, a lessee should reallocate contract consideration, reassess the lease classification, remeasure the lease liability, and adjust the right-of-use asset.

**Research and Development Expense**

Research and development expense consists of expenses incurred in performing research and development activities including related salaries, clinical trial and related drug and non-drug product costs, contract services and other outside service expenses. Research and development expense is charged to operating expense in the period incurred.

**Clinical Trial Accruals**

Clinical trial costs are a component of research and development expenses. The Company accrues and expenses clinical trial activities performed by third parties based upon actual work completed in accordance with agreements established with clinical research organizations and clinical sites. The Company determines the costs to be recorded based upon validation with the external service providers as to the progress or stage of completion of trials or services and the agreed-upon fee to be paid for such services.

**Revenue Recognition**

The Company recognizes revenue in accordance with ASC Topic 606, *Revenue from Contracts with Customers* ("ASC 606").

The Company's policy typically permits returns if the product is damaged, defective, or otherwise cannot be used when received by the customer if the product has expired. Returns are accepted for product that will expire within six months or that have expired up to one year after their expiration dates. Estimates for expected returns of expired products are based primarily on an ongoing analysis of our historical return patterns.

The Company recognizes revenue in accordance with the core principle of ASC 606 or when there is a transfer of control of promised goods to customers in an amount that reflects the consideration that the Company expects to be entitled to in exchange for those goods.

The Company recognizes the incremental costs of obtaining a contract as an expense when incurred if the amortization period of the asset that the Company otherwise would have recognized is one year or less.

The Company does not adjust the amount of consideration for the effects of a significant financing component if, at contract inception, the expected period between the transfer of promised goods and customer payment is one year or less.

The Company has elected to treat shipping and handling activities as fulfillment costs.

Additionally, the Company elected to record revenue net of sales and other similar taxes.

**Contracts and Agreements**

The Company's Canalevia-CA1 and Neonorm products are primarily sold to distributors, who then sell the products to the end customers. Since 2021, the Company has entered into two distribution agreements with established distributors to distribute the Company's animal health products in the US. The distribution agreements and the related purchase orders together meet the contract existence criteria under ASC 606-10-25-1. The Company sells directly to its customers without the use of an agent.

*Performance obligations*

For animal health products sold by the Company, the single performance obligation identified above is the Company's promise to transfer the Company's animal health products to distributors based on specified payment and shipping terms in the arrangement. Product warranties are assurance-type warranties that do not represent a performance obligation. For the Company's human health product, Mytesi, the single performance obligation identified above is the Company's promise to transfer Mytesi to specialty pharmacies, based on specified payment and shipping terms as outlined in the Exclusive Distribution Agreement entered into by the Company and Cardinal Health on January 16, 2019.

*Transaction price*

For contracts with Cardinal Health and other distributors, the transaction price is the amount of consideration to which the Company expects to collect in exchange for transferring the promised goods or services. The transaction price of Mytesi is the Wholesaler Acquisition Cost ("WAC"), and the transaction price of Canalevia-CA1 and Neonorm is the manufacturer's list price, net of discounts, returns, and price adjustments.

*Allocate transaction price*

For contracts with Cardinal Health and other distributors, the entire transaction price is allocated to the single performance obligation contained in each contract.

*Revenue recognition*

For contracts with Cardinal Health, for the Company, a single performance obligation is satisfied at a point in time, upon the FOB terms of each contract when control, including title and all risks, has transferred to the customer.

*Disaggregation of Product Revenue*

Human

Sales of Mytesi are recognized as revenue at a point in time when the products are delivered to the wholesaler. Net revenues from the sale of Mytesi were \$ 9.6 million and \$ 11.7 million for the years ended December 31, 2023 and 2022, respectively.

#### Animal

The Company recognized Canalevia-CA1 products revenues of \$ 130,000 and \$ 167,000 for the years ended December 31, 2023 and 2022, respectively. The Company recognized Neonorm revenues of \$ 42,000 and \$ 48,000 for the years ended December 31, 2023 and 2022, respectively. Revenues are recognized at a point in time upon shipment, which is when title and control is transferred to the buyer. Sales of Canalevia-CA1, Neonorm Calf and Foal to distributors are made under agreements that may provide distributor price adjustments and rights of return under certain circumstances.

#### ***Contracts – Specialty Pharmacies***

Effective October 1, 2020, the Company engaged a private company as its third-party logistics distribution agent for commercial sales of the Company's Mytesi product. Under the Specialty Product Distribution Agreement, the Company shall supply the products to the private company's specialty pharmacies, through a designated wholesaler, in such amounts as may be ordered. There is no minimum purchase or inventory requirement. The specialty pharmacies were authorized distributors of record for all National Drug Codes ("NDCs") of Mytesi.

Effective April 20, 2021, the Company engaged another private company as an authorized specialty pharmacy provider of Mytesi. Under the Specialty Pharmacy Distribution and Services Agreement, the private company shall sell and dispense the Mytesi directly ordered from the Company at the agreed price to patients within the territories identified in the agreement.

The Company has entered into agreements with a total of five different specialty pharmacy chains that are authorized to provide Mytesi to patients.

#### *Performance obligations*

The single performance obligation is the Company's promise to transfer Mytesi to specialty pharmacies, based on specified payment and shipping terms outlined in the agreements.

#### *Transaction price*

The transaction price is the amount of consideration to which the Company expects to collect in exchange for transferring the promised goods or services. The transaction price of Mytesi is the WAC, net of estimated discounts, returns, and price adjustments.

#### *Allocate transaction price*

The entire transaction price is allocated to the single performance obligation contained in each contract.

#### *Revenue recognition*

The single performance obligation is satisfied at a point in time, upon the free on board ("FOB") terms of each contract, when control, including title and all risks, has transferred to the customer.

#### *Product Revenue*

Sales of Mytesi are recognized as revenue at a point in time when the products are delivered to the specialty pharmacies. Net revenues from the sale of Mytesi to the specialty pharmacies were \$ 8.1 million and \$ 10.3 million for the years ended December 31, 2023 and 2022, respectively.

### **Collaboration Revenue**

Revenue recognition for collaboration agreements requires significant judgment. The Company's assessments and estimates are based on contractual terms, historical experience and general industry practice. Revisions in these values or estimations have the effect of increasing or decreasing collaboration revenue in the period of revision.

On September 24, 2018, the Company entered into a Distribution, License and Supply Agreement ("License Agreement") with Knight Therapeutics ("Knight"). The License Agreement has a term of 15 years (with automatic renewals) and provides Knight with an exclusive right to commercialize current and future Jaguar human health products (including crofelemer, NP-300, and any product containing a proanthocyanidin or with an anti-secretory mechanism) in Canada and Israel. Knight forfeited its right of first negotiation for expansion to Latin America. Under the License Agreement, Knight is responsible for applying for and obtaining necessary regulatory approvals in the territory of Canada and Israel, as well as marketing, sales and distribution of the licensed products. Knight will pay a transfer price for all licensed products, and upon achievement of certain regulatory and sales milestones, the Company may receive payments from Knight in an aggregate amount of up to approximately \$ 18 million payable throughout the initial 15 -year term of the agreement. The Company did not have any significant license revenues for the years ended December 31, 2023 and 2022.

### **Modifications to Liability-classified Instruments**

In accounting for debt modifications and exchange transactions, it is the Company's policy to first determine whether it qualifies as a Troubled Debt Restructuring ("TDR") pursuant to the guidance provided in ASC 470-60. A debt modification or exchange transaction that is not within the scope of the ASC 470-60 is accounted for under ASC 470-50 to determine if the transaction is a mere modification or an extinguishment.

For the year ended December 31, 2023, the Company entered amendments to the terms of the October 2020 Royalty Interest, December 2020 Royalty Interest, and August 2022 Royalty Interest.

For the year December 31, 2022, the Company entered into another amendment on the terms of its October 2020 and March 2021 Purchase Agreements.

The cumulative impact of these amendments significantly modified the terms of the royalty interest resulting to extinguishments (see Note 7).

### **Modifications to Equity-classified Instruments**

In accounting for modifications of equity-classified warrants, it is the Company's policy to determine the impact by analogy to the share-based compensation guidance of ASC 718, *Compensation - Stock Compensation* ("ASC 718"). The model for a modified share-based payment award that is classified as equity and remains classified in equity after the modification is addressed in ASC 718-20-35-3. Pursuant to that guidance, the incremental fair value from the modification is recognized as an expense in the statements of operations to the extent the modified instrument has a higher fair value; however, in certain circumstances, such as when an entire class of warrants are modified, the measured increase in fair value may be more appropriately recorded as a deemed dividend, depending upon the nature of the warrant modification.

The Company did not modify any equity-classified warrants in the year 2023 and 2022.

In accounting for amendments to equity-classified preferred stock, it is the Company's policy to measure the impact by analogy to ASC 470-50 in determining if such an amendment is an extinguishment or a modification. If the amendment results in an extinguishment, the Company follows the SEC staff guidance in ASC 260-10-S99-2 and ASC 470-20. If the amendment results in a modification, the Company follows the model in either ASC 718 or ASC 470-50, depending on the nature of the amendment.

The Company did not modify any equity-classified preferred stock in the years 2023 and 2022.

**Stock-Based Compensation**

The Company's Stock Incentive Plan (see Note 11) provides for the grant of stock options, restricted stock and restricted stock unit awards. The Company measures stock awards granted to employees, non-employees and directors at estimated fair value on the date of grant and recognizes the corresponding compensation expense of the awards, net of estimated forfeitures, over the requisite service periods, which correspond to the vesting periods of the awards. Forfeitures are estimated at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from those estimates. The Company issues stock awards with only service-based vesting conditions, and records compensation expense for these awards using the straight-line method.

The Company uses the grant date fair market value of its common stock to determine the grant date fair value of options granted to employees, non-employees and directors. The Company measures and recognizes compensation expense for all stock options and restricted stock units ("RSUs") granted to its employees and directors based on the estimated fair value of the award on the grant date. The Company uses the Black-Scholes valuation model to estimate the fair value of stock option awards. The fair value is recognized as expense, net of estimated forfeitures, over the requisite service period, which is generally the vesting period of the respective award, on a straight-line basis. The Company believes that the fair value of stock options granted to non-employees is more reliably measured than the fair value of the services received. The determination of the grant date fair value of options using an option pricing model is affected by the Company's estimated Common Stock fair value and requires management to make a number of assumptions including the expected life of the option, the volatility of the underlying stock, the risk-free interest rate and expected dividends.

The Company estimates the fair value of stock options using the Black-Scholes option valuation model. The fair value of employee stock options is being amortized on a straight-line basis over the requisite service period of the awards. The fair market value of common stock is based on the closing price of the Company's common stock as reported on the date of the grant.

**Income Taxes**

The Company uses the asset and liability method of accounting for income taxes. Under this method, deferred tax assets and liabilities are determined based on the differences between the financial reporting and the tax bases of assets and liabilities and are measured using the enacted tax rates and laws that will be in effect when the differences are expected to reverse. A valuation allowance is provided when it is more likely than not that some portion or all of a deferred tax asset will not be realized.

The Company has adopted the provisions of ASC 740, *Income Taxes Related to Uncertain Tax Positions*. Under these principles, tax positions are evaluated in a two-step process. The Company first determines whether it is more-likely-than-not that a tax position will be sustained upon examination. If a tax position meets the more-likely-than-not recognition threshold, it is then measured to determine the amount of benefit to be recognized in the financial statements. The tax position is measured as the largest amount of benefit that has a greater than 50 percent likelihood of being realized upon ultimate settlement.

**Foreign Currency Remeasurement and Translation**

The functional currency of Napo Therapeutics is Euro. The Company follows ASC 830, *Foreign Currency Matters* ("ASC 830"). ASC 830 requires the assets, liabilities, and results of operations of a foreign operation to be measured using the functional currency of that foreign operation. Exchange gains or losses from remeasuring transactions and monetary accounts in a currency other than the functional currency are included in current earnings.

For certain subsidiaries, translation adjustments resulting from the process of translating the functional currency of subsidiary financial statements into the US Dollar reporting currency. These translation adjustments are

reported separately and accumulated in the consolidated balance sheets as a component of accumulated other comprehensive income (loss).

#### **Comprehensive Loss**

The Company follows ASC 220, *Comprehensive Income*, which establishes standards for reporting and displaying comprehensive income and its components (revenue, expenses, gains and losses) in a full set of general-purpose financial statements.

For the years ended December 31, 2023 and 2022, the amount of other comprehensive income (loss) from translation adjustments were \$ 31,000 and (\$ 680,000 ), respectively.

#### **Basic and Diluted Net Loss Per Common Share**

Basic net loss per common share is computed by dividing net loss attributable to common stockholders for the year by the weighted-average number of common shares outstanding during the year. Diluted net loss per share is computed by dividing the net loss attributable to common stockholders for the year by the weighted-average number of common shares, including potential dilutive shares of common stock assuming the dilutive effect of potential dilutive securities. For years in which the Company reports a net loss, diluted net loss per common share is the same as basic net loss per common share, because their impact would be anti-dilutive to the calculation of net loss per common share. Diluted net loss per common share is the same as basic net loss per common share for the years ended December 31, 2023 and 2022.

#### **Recent Accounting Pronouncements**

##### *Recently Adopted Accounting Pronouncements*

In June 2016, the FASB issued ASU 2016-13, Financial Instruments – Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments. The main objective of the standard is to provide financial statement users with more decision-useful information about the expected credit losses on financial instruments and other commitments to extend credit held by a reporting entity at each reporting date. To achieve this objective, the amendments in this standard replace the incurred loss impairment methodology in current GAAP with a methodology that reflects expected credit losses and requires consideration of a broader range of reasonable and supportable information to inform credit loss estimates. The update is effective for the Company beginning January 1, 2023 with early adoption permitted. The Company adopted the standard on January 1, 2023. The adoption of this standard did not have a material effect on the Company's audited consolidated financial statements and related disclosures.

##### *Recently Issued Accounting Pronouncements Not Yet Adopted*

In October 2023, the FASB issued ASU 2023-06—Codification Amendments in Response to the SEC's Disclosure Update and Simplification Initiative. The main objective of the amendment is to modify the disclosure or presentation requirements of various Topics in the Codification. Certain amendments represent clarifications to or technical corrections of the current requirements. to eliminate disclosure requirements that were redundant, duplicative, overlapping, outdated, or superseded. The effective date for each amendment will be when the SEC's removal of that related disclosure from Regulation S-X or Regulation S-K becomes effective, with early adoption prohibited. The Company is still evaluating the impact of the adoption of this standard.

#### **3. Fair Value Measurements**

ASC 820, *Fair Value Measurements* ("ASC 820"), defines fair value, establishes a framework for measuring fair value under US GAAP and enhances disclosures about fair value measurements. Fair value is defined under ASC 820 as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants

on the measurement date. Valuation techniques used to measure fair value under ASC 820 must maximize the use of observable inputs and minimize the use of unobservable inputs. The standard describes a fair value hierarchy based on three levels of inputs, of which the first two are considered observable and the last unobservable, that may be used to measure fair value which are the following:

- Level 1 – Observable inputs such as quoted prices (unadjusted) for identical instruments in active markets.
- Level 2 – Observable inputs such as quoted prices for similar instruments in active markets, quoted prices for identical or similar instruments in markets that are not active, or model -derived valuations whose significant inputs are observable.
- Level 3 – Unobservable inputs that reflect the reporting entity's own assumptions.

The following tables set forth the fair value of the Company's consolidated financial instruments that were measured at fair value as of December 31, 2023 and 2022:

(in thousands)	December 31, 2023				Total
	Level 1	Level 2	Level 3		
Iliad	\$ —	\$ —	\$ 6,862	\$ 6,862	\$ 6,862
Uptown	—	—	7,473	7,473	7,473
Streeterville 2	—	—	6,815	6,815	6,815
Streeterville Note	—	—	9,793	9,793	9,793
<b>Total fair value</b>	<b>\$ —</b>	<b>\$ —</b>	<b>\$ 30,943</b>	<b>\$ 30,943</b>	<b>\$ 30,943</b>

(in thousands)	December 31, 2022				Total
	Level 1	Level 2	Level 3		
Streeterville Note	\$ —	\$ —	\$ 7,839	\$ 7,839	\$ 7,839
<b>Total fair value</b>	<b>\$ —</b>	<b>\$ —</b>	<b>\$ 7,839</b>	<b>\$ 7,839</b>	<b>\$ 7,839</b>

The change in the estimated fair value of the Level 3 liabilities is summarized below:

(in thousands)	Year Ended December 31, 2023			
	Iliad	Uptown	Streeterville 2	Streeterville Note
Beginning fair value of Level 3 liability	\$ —	\$ —	\$ —	\$ 7,839
Additions	6,580	7,478	6,154	—
Exchanges	( 789 )	—	—	—
Settlements	—	( 1,444 )	—	—
Change in fair value	1,071	1,439	661	1,954
<b>Ending fair value of Level 3 liability</b>	<b>\$ 6,862</b>	<b>\$ 7,473</b>	<b>\$ 6,815</b>	<b>\$ 9,793</b>

(in thousands)	Year Ended December 31, 2022			
	Iliad	Uptown	Streeterville 2	Streeterville Note
Beginning fair value of Level 3 liability	\$ —	\$ —	\$ —	\$ 7,819
Additions	—	—	—	—
Settlements	—	—	—	—
Change in fair value	—	—	—	20
<b>Ending fair value of Level 3 liability</b>	<b>\$ —</b>	<b>\$ —</b>	<b>\$ —</b>	<b>\$ 7,839</b>

The fair value of the Streeterville Note recognized as a Level 3 liability at the date of issuance and as of December 31, 2023 amounted to \$ 7.8 million and \$ 9.8 million, respectively. The fair value of the remaining Level 3 liabilities at the election date and as of December 31, 2023 amounted to \$ 20.2 million and \$ 21.0 million. The fair values were based on the weighted average discounted expected future cash flows representing the terms of the notes, discounting them to their present value equivalents. The notes were classified as Level 3 fair values in the fair value hierarchy due to the use of unobservable inputs, including the Company's own credit risk.

The Company determined and performed the valuations with the assistance of an independent valuation service provider. On a quarterly basis, the Company considers the main Level 3 inputs for the hybrid instrument used derived as follows:

- Discount rate which was determined using a comparison of various effective yields on bonds as of the valuation date
- Market indications for vouchers, which affect the Return Bonus from the sale of Tropical Disease Priority Review Voucher ("TDPRV")
- Weighted probability of cash outflows which was estimated based on the entity's knowledge of the business and how the current economic environment is likely to impact the timing of the cash outflows, attributed to the different repayment features of the notes.

The following table summarizes the quantitative information about the significant unobservable inputs used in Level 3 fair value measurement of the hybrid instrument:

Unobservable Inputs	Range of Inputs (probability-weighted average)		Relationship of unobservable inputs to fair value
	2023	2022	
Risk Adjusted Discount Rate	9.02 %- 24.59 % (24.59 %)	11.53 %- 26.06 % (26.06 %)	If discount rate is adjusted to total of additional 100 basis points (bps), fair value would have decreased by \$ 398,000 .
Sales Proceeds: Amount of comparable TDPRV	\$ 67.5 million to \$ 350 million (\$ 100 million)	\$ 67.5 million to \$ 350 million (\$ 100 million)	If discount rate is adjusted to total deduction of 100 bps, fair value would have increased by \$ 398,000 .
Range of Probability for Timing of Cash Flows: Variations of the terms and conditions of the timing of cash flows, including settlement of the note principal, interest, penalties, and acceleration clause.	0.10 %- 73.27 %	0.39 %- 46.55 %	If expected cash flows by Management considered the lowest amount of market indications for vouchers, FV would have decreased by \$ 1.34 million.  If expected cash flows by Management considered the highest amount of market indications for vouchers, FV would have increased by \$ 10.38 million.  If expected cash flows by Management considered the Scenario with the least amount of indicated value, FV would have decreased by \$ 227,000 .  If expected cash flows by Management considered the scenario with the greatest amount of indicated value, FV would have increased by \$ 3.18 million.

For the additional notes designated at FVO that are freestanding, the Company considers only the discount rate which was determined using a comparison of various effective yields on bonds as of valuation date.

The following table summarizes the quantitative information about the significant unobservable inputs used in Level 3 fair value measurement for the remaining instruments that are classified as freestanding:

Unobservable Inputs	Range of Inputs (probability-weighted average)		Relationship of unobservable inputs to fair value
	2023	2022	
Risk Adjusted Discount Rate	9.02 %- 26.59 % ( 26.59 %)	—	If discount rate is adjusted to total of additional 100 basis points (bps), fair value would have decreased by (\$ 583,464 ).  If discount rate is adjusted to total deduction of 100 bps, fair value would have increased by \$ 600,531 .

#### **Fair Value Option**

The Company elected to apply the FVO accounting to certain freestanding instruments and to the entire class of hybrid instruments, including structured notes, of which there are assessed embedded derivatives that would be eligible for bifurcation, to align the measurement attributes of those instruments under US GAAP and to simplify the accounting model applied to these financial instruments.

The valuations of these instruments were predominantly driven by the discount rate and the derivative features embedded within the instruments. The Company determined and performed the valuations of the freestanding and hybrid instruments with the assistance of an independent valuation service provider. The valuation methodology utilized is consistent with the income approach for estimating the fair value of the interest-bearing portion of the instruments and the related derivatives. Cash flows of the financial instruments in their entirety, including the embedded derivatives, are discounted at an appropriate rate for the applicable duration of the instrument.

Interests on the interest-bearing portion of the instruments that are held to maturity and mark-to-market adjustments are aggregated in the change in fair value of freestanding and hybrid financial instruments designated at FVO in the consolidated statements of operations.

For the year ended December 31, 2023 and 2022, the Company did not note any fair value movement on FVO liabilities attributable to any instrument-specific credit risk, which should be recorded in other comprehensive income (loss).

The following table summarizes the fair value and unpaid principal balance for items the Company accounts under FVO:

(in thousands)	Fair value	Unpaid Principal Balance	Accrued Interest	Fair Value Over (Under) Outstanding Balance
<b>At December 31, 2023</b>				
Iliad	\$ 6,862	\$ 7,292	\$ 3,621	\$ ( 4,051 )
Uptown	7,473	7,994	4,058	( 4,579 )
Streeterville 2	6,815	10,273	950	( 4,408 )
Streeterville Note	9,793	6,000	546	3,247
(in thousands)	Fair value	Unpaid Principal Balance	Accrued Interest	Fair Value Over (Under) Outstanding Balance
<b>At December 31, 2022</b>				
Streeterville Note	\$ 7,839	\$ 6,000	\$ 390	\$ 1,449

#### 4. Related Party Transactions

##### *BOD Cash Compensation*

The Company makes BOD cash compensation on a quarterly basis based on the Director Compensation Program. For the years ended December 31, 2023, and 2022, the Company paid approximately \$ 498,000 and \$ 411,000 cash compensation to its directors.

## 5. Commitments and Contingencies

### ***Commitments***

#### ***Leases***

On April 6, 2021, the Company entered into an office lease agreement of approximately 10,526 square feet of office space in San Francisco, inclusive of office space covered under the previous sublease agreement. The term of the lease began on September 1, 2021 and will expire on February 28, 2025, unless terminated earlier. The lease had an early occupancy provision which entitled the Company to use a portion of the leased premises on June 1, 2021, free of rent obligation. In addition, the Company has the option to extend the lease for one three-year period after the expiration date. This option was not included as part of the lease term as the Company was not reasonably certain to exercise it, hence the lease term only includes the noncancellable period of three years plus the period of early occupancy.

The base rents under the lease were \$ 42,000 monthly for the first 12 months, \$ 43,000 monthly for the next 12 months and \$ 45,000 for the last twelve months. The lease agreement only contained one lease component, that is, the lease of the office space. Non-lease components such as payment of building operating costs and share in real property taxes were accounted for separately and were not considered as part of the total lease payments. The lease was classified as an operating lease.

On October 7, 2021, the Company entered into an agreement for the lease of office premises, one located on the 4<sup>th</sup> floor of the building ("Suite 400") and the other one on the 6<sup>th</sup> floor ("Suite 600"), from November 1, 2021 to April 30, 2022, subject to automatic renewal for subsequent periods until terminated by either party. Base rent amounted to € 10,000 or approximately \$ 10,500. If the contract is not terminated within 12 months, the lease amount will be increased in line with the index of relevant inflation at each annual expiration of the start date of the contract. The lessor has the right to decline the renewal of the contract. Upon the happening of certain specified events, the lessor may immediately withdraw from the contract. The Company is required to leave the occupied spaces immediately in the same condition in which they were found in the event of contract termination or expiry. The Company paid a deposit of € 20,000, or approximately \$ 21,000, to the lessor. On January 26, 2022, the lease agreement was amended whereby the term was extended by 20 months from May 1, 2022 to December 31, 2023. All other contract provisions remained the same.

On October 25, 2023, the Company entered into a second amendment to extend the lease of the office premises whereby Suite 600 shall extend until February 28, 2025, while, the Suite 400 shall be accounted for as a separate lease commencing on September 1, 2023, and expiring on August 31, 2030. Under the second lease amendment, the office lease premises were separately remeasured with Suite 400 measuring approximately 5,735 square feet while Suite 600 at 5,263 square feet. The base rent for Suite 400 was \$ 18,000 monthly on the first two years, \$ 18,000 monthly on the third and fourth year, \$ 19,000 monthly on the fifth and sixth year, \$ 20,000 monthly on the seventh and eighth year and \$ 21,000 on the last year. Accordingly, the Suite 600's base rent was amended into \$ 22,000 monthly on its remaining terms. The option to renew at the end of the lease term was amended into one-to- five-year period from the original one-to- three-year period. All other contract provisions remained the same.

On October 10, 2021, the Company also entered into a short-term office lease in Milan, Italy. The term of the lease began on November 1, 2021, subject to automatic renewal equal to the present term until terminated by mutual agreement. On January 26, 2022, the lease agreement was amended whereby the term was extended by 20 months from May 1, 2022 to December 31, 2023. On September 12, 2023, the Company entered into a second lease amendment whereby the term was extended by another year from January 1, 2024 to December 31, 2024. The Company recognizes rent expense on a straight-line basis over the non-cancellable lease period.

On December 22, 2021, the Company entered into an agreement for the lease of two separate vehicles for 48 months expiring on November 30, 2025. Total monthly lease payment amounted to € 2,000 or approximately \$ 2,100 payable in advance. The Company elected to include both the lease and non-lease components as a single component and account for it as a lease. The Company also paid a total deposit of € 19,000 or approximately \$ 20,000, exclusive of VAT. Early termination of the contracts requires the payment of specified amounts.

On January 25, 2022, the Company entered into an agreement for the lease of office premises from March 1, 2022 to December 31, 2023, subject to automatic renewal for subsequent periods until terminated by either party. Base rent amounted to € 4,000 or approximately \$ 4,200. A similar agreement was entered with the lessor for the lease of premises to be used as office space from November 1, 2022 to December 31, 2023, subject to automatic renewal for subsequent periods until terminated by either party. Base rent amounted to € 3,817 or approximately \$ 4,000. If the contracts are not terminated within 12 months, the lease amounts will be increased in line with the index of relevant inflation at each annual expiration of the start date of the contract. The lessor has the right to decline the renewal of the contracts. Upon the happening of certain specified events, the lessor may immediately withdraw from the contracts. The Company is required leave the occupied spaces immediately in the same conditions in which they were found in the event of contract termination or expiry. The Company paid a deposit of € 9,000 or approximately \$ 9,500 to the Lessor.

In May 2022, the Company entered into an agreement for the lease of one vehicle for 48 months expiring on April 30, 2026. Total monthly lease payment amounted to € 833 or approximately \$ 880 payable in advance. The Company elected to include both the lease and non-lease components as a single component and account for it as a lease. The Company also paid a total deposit of € 21,000 or approximately \$ 22,000, exclusive of VAT. Early termination of the contracts requires the payment of specified amounts.

In October 2022, the Company entered into an agreement for the lease of three vehicles for 48 months expiring on September 30, 2026. Total monthly lease payment amounted to € 2,094 or approximately \$ 2,200 payable in advance. The Company elected to include both the lease and non-lease components as a single component and account for it as a lease.

In November 2022, the Company entered into an agreement for the lease of two vehicles for 48 months expiring on October 31, 2026. Total monthly lease payment amounted to € 1,459 or approximately \$ 1,500 payable in advance. The Company elected to include both the lease and non-lease components as a single component and account for it as a lease.

[Table of Contents](#)

The table below provided additional details of the office space lease presented in the consolidated balance sheet:

	<u>December 31, 2023</u>	<u>December 31, 2022</u>
(in thousands)		
Operating lease - right-of-use asset	\$ 1,176	\$ 1,140
Operating lease liability, current	348	483
Operating lease liability, net of current portion	886	725
Total	<u>\$ 1,234</u>	<u>\$ 1,208</u>
Weighted-average remaining life (years)	1.71	2.36
Weighted-average discount rate	<u>16.82 %</u>	<u>17.89 %</u>

Lease cost included in general and administrative expenses in the consolidated statements of operations for the years ended December 31, 2023 and 2022 was approximately \$ 821,000 and \$ 629,000 .

For the years ended December 31, 2023 and 2022, cash paid for operating lease liabilities recognized under operating cash flows amounted to \$ 394,000 and \$ 315,000 , respectively. Non-cash investing and financing activities for the years ended December 31, 2023 and 2022 include addition to right-of-use asset obtained from new operating liabilities amounting to \$ 30,000 and \$ 365,000 , respectively, and lease modification amounting to \$ 441,000 and zero respectively.

The following table summarizes the undiscounted cash payment obligations for the operating lease liability:

	<u>December 31, 2023</u>
(in thousands)	
2024	\$ 562
2025	346
2026	266
2027	233
2028	240
2029	247
2030	168
Total undiscounted operating lease payments	2,062
Imputed interest expenses	( 828 )
Total operating lease liability	1,234
Less: Operating lease liability, current	348
Operating lease liability, net of current portion	<u>\$ 886</u>

*Purchase Commitment*

On September 3, 2020, the Company entered into a manufacturing and supply agreement (the "Agreement") with Glenmark Life Sciences Limited ("Glenmark"), pursuant to which Glenmark will continue to serve as the Company's manufacturer of crofelemer for use in Mytesi, the Company's human prescription drug product approved by the US Food and Drug Administration, and for other crofelemer-based products manufactured by the Company or its affiliates for human or animal use. The term of the Agreement is approximately 2.5 years (i.e., until March 31, 2023) and may be extended for successive two-year renewal terms upon mutual agreement between the parties

thereto. Pursuant to the terms of the Agreement, Glenmark will supply crofelemer to the Company. The Agreement contains provisions regarding the rights and responsibilities of the parties with respect to manufacturing specifications, forecasting and ordering, delivery arrangements, payment terms, confidentiality and indemnification, as well as other customary provisions. The Agreement includes a commitment for the purchase from Glenmark of a minimum quantity of 500 kilograms of crofelemer per year, pro-rated for partial years, where the Company may be obligated to pay any shortfall. Either party may terminate the Agreement for any reason with 12 months prior written notice to the other party. In addition, either party may terminate the Agreement upon written notice as a result of a material breach of the Agreement that remains uncured for a period of 90 days. If the Company terminates the Agreement as a result of a material breach caused by Glenmark, the Company will not be obligated to pay for any minimum quantity shortfall. As of December 31, 2023, the remaining commitment is 125 kilograms.

*Master Services Agreement ("MSA")*

On October 5, 2020, the Company entered into another MSA for clinical research organization services (the "2020 MSA") and a service order under such 2020 MSA with Integrium. The service order covers the Company's planned upcoming pivotal Phase 3 clinical trial for cancer-therapy related diarrhea. As consideration for its services, the Company will pay Integrium a total amount of up to approximately \$ 12.4 million that will be paid over the term of the engagement and based on the achievement of certain milestones. The 2020 MSA will terminate upon the satisfactory performance of all services to be provided thereunder unless earlier terminated by the parties. For the years ended December 31, 2023 and 2022, the Company paid Integrium \$ 1.8 million and \$ 1.9 million, respectively.

*Asset Transfer and Transition Commitment*

On September 25, 2017, Napo entered into the Termination, Asset Transfer and Transition Agreement dated September 22, 2017 with Glenmark. As a result of the agreement, Napo now controls commercial rights for Mytesi for all indications, territories and patient populations globally, and also holds commercial rights to the existing regulatory approvals for crofelemer in Brazil, Ecuador, Zimbabwe and Botswana. In exchange, Napo agrees to pay Glenmark 25 % of any payment it receives from a third party to whom Napo grants a license or sublicense or with whom Napo partners in respect of, or sells or otherwise transfers any of the transferred assets, subject to certain exclusions, until Glenmark has received a total of \$ 7.0 million. For the years ended December 31, 2023 and 2022, the Company paid Glenmark \$ 3.0 million and \$ 2.6 million, respectively.

*Revenue Sharing Commitment Update*

On December 14, 2017, the Company announced its entry into a collaboration agreement with Seed Mena Businessmen Services LLC ("SEED") for Equilevia™, the Company's non-prescription, personalized, premium product for total gut health in equine athletes. According to the terms of the Agreement, the Company will pay SEED 15 % of total revenue generated from any clients or partners introduced to the Company by SEED in the form of fees, commissions, payments or revenue received by the Company or its business associates or partners, and the agreed-upon revenue percentage increases to 20 % after the first million dollars of revenue. In return, SEED will provide the Company access to its existing United Arab Emirates ("UAE") network and contacts and assist the Company with any legal or financial requirements. The agreement became effective on December 13, 2017 and will continue indefinitely until terminated by either party pursuant to the terms of the Agreement. No payments have been made to date.

*Joint Venture - Magdalena Biosciences, Inc.*

In January 2023, Jaguar and Filament Health ("Filament"), with Funding from One Small Planet, formed the US-based joint venture Magdalena Biosciences, Inc. ("Magdalena"). Magdalena's focus is on the development of novel, natural prescription medicines derived from plants for mental health indications including, initially, attention-deficit/hyperactivity disorder ("ADHD") in adults. The goal of the collaboration is to extend the botanical drug development capabilities of Jaguar and Filament in order to develop pharmaceutical-grade, standardized drug candidates for mental health disorders, and to partner with a potential future licensee to develop and commercialize these novel plant-based drugs. This venture aligns with Jaguar's mental health Entheogen Therapeutics Initiative ("ETI") and Filament's corporate mission to develop novel, natural prescription medicines from plants. Magdalena

will leverage Jaguar's proprietary medicinal plant library and Filament's proprietary drug development technology. Jaguar's library of 2,300 highly characterized medicinal plants and 3,500 plant extracts, all from firsthand ethnobotanical investigation by Jaguar and members of the ETI Scientific Strategy Team, is a key asset Jaguar has generated over 30 years that bridges the knowledge of traditional healers and Western medicine. Magdalena holds an exclusive license to plants and plant extracts in Jaguar's library, not including any sources of crofelemer or NP-300, for specific indications and is in the process of identifying plant candidates in the library that may prove beneficial for addressing indications such as ADHD.

The Company accounted for its 40 % investment in Magdalena under the equity method. The summarized income statement information for the year ended December 31, 2023 of Magdalena is as follows:

	Year ended December 31, 2023
(in thousands)	
Revenue	\$ —
Operating expenses	( 128 )
Loss before income tax	( 128 )
Income tax expense	—
Net loss	\$ ( 128 )
Net loss attributable to the Company	<u><u>\$ ( 51 )</u></u>

#### **Contingencies**

From time to time, the Company maybe a party to various legal actions, both inside and outside the US, arising in the ordinary course of its business or otherwise. The Company accrues amounts, to the extent they can be reasonably estimated, that the Company believes will result in a probable loss (including, among other things, probable settlement value), to adequately address any liabilities related to legal proceedings and other loss contingencies. A loss or a range of loss is disclosed when it is reasonably possible that a material loss will incur and can be estimated, or when it is reasonably possible that the amount of a loss, when material, will exceed the recorded provision. The Company did not have any material accruals for any currently active legal action in its consolidated balance sheets as of December 31, 2023, as the Company could not predict the ultimate outcome of these matters, or reasonably estimate the potential exposure.

#### **6. Balance Sheet Components**

##### ***Inventory***

Inventory at December 31, 2023 and 2022 consisted of the following:

	December 31, 2023	December 31, 2022
(in thousands)		
Raw material	\$ 2,057	\$ 2,101
Work in process	6,517	3,599
Finished goods	615	1,324
Inventory	<u><u>\$ 9,189</u></u>	<u><u>\$ 7,024</u></u>

*Prelaunch Inventory*

Costs capitalized for the Company's lyophilized drug amounting to \$ 2.8 million and \$ 2.1 million as of December 31, 2023, and 2022 are included in the prepayments and other assets account. The Company's proof-of-concept ("POC") data is expected to be completed by the end of 2024. Upon approval, the prelaunch inventory shall be reclassified as part of the Company's inventory.

**Property and Equipment, net**

Property and equipment at December 31, 2023 and 2022 consisted of the following:

	December 31, 2023	December 31, 2022
(in thousands)		
Land	\$ 396	\$ 396
Lab equipment	477	477
Software	63	63
Furniture and fixtures	18	18
Computers and peripherals	7	7
Total property and equipment at cost	961	961
Accumulated depreciation	(465)	(404)
Property and equipment, net	<u>\$ 496</u>	<u>\$ 557</u>

Depreciation and amortization expense was \$ 61,000 and \$ 171,000 for the years ended December 31, 2023 and 2022, respectively.

**Intangible assets, net**

Intangible assets, net of amortization, at December 31, 2023 and 2022 consisted of the following:

	December 31, 2023	December 31, 2022
(in thousands)		
Developed technology	\$ 25,000	\$ 25,000
Accumulated developed technology amortization	( 10,694)	( 9,028)
Developed technology, net	<u>14,306</u>	<u>15,972</u>
In-process research and development	4,800	4,800
In process research and development, net	4,800	4,800
Trademarks	300	300
Accumulated trademark amortization	( 128)	( 108)
Trademarks, net	<u>172</u>	<u>192</u>
Internal use software costs - registry	1,236	1,236
Accumulated internal use software costs impairment	( 371)	—
Accumulated internal use software costs amortization	( 370)	( 122)
Internal use software costs - registry, net	<u>495</u>	<u>1,114</u>
Patents	361	361
Accumulated patents amortization	( 18)	—
Patents, net	<u>343</u>	<u>361</u>
Total intangible assets, net	<u>\$ 20,116</u>	<u>\$ 22,439</u>

Amortization expense of finite-lived intangible assets was \$ 2.0 million and \$ 1.8 million for the years ended December 31, 2023 and 2022, respectively.

During 2023, the Company experienced lower-than-anticipated sales growth for Canalevia and Neonorm, its two primary animal health products. This triggered a reevaluation of the carrying value of the entire asset group associated with these products. Based on the evaluation, the Company determined that the internal use software costs - registry carrying value of \$ 866,000 , was no longer recoverable. For the year ended December 31, 2023, The Company wrote the internal use software costs – registry down to its estimated fair value of \$ 495,000 and recognized an impairment loss on intangible asset of \$ 371,000 . No assets were determined to be impaired as at December 31, 2022.

The following table summarizes the Company's estimated future amortization expense of intangible assets with finite lives as of December 31, 2023:

(in thousands)	Amounts
2024	\$ 1,952
2025	1,952
2026	1,952
2027	1,952
2028	1,952
Thereafter	5,556
	<u>\$ 15,316</u>

#### **Accrued Liabilities**

Accrued liabilities at December 31, 2023 and 2022 consisted of the following:

(in thousands)	December 31, 2023	December 31, 2022
Accrued interest	\$ 719	\$ 5,489
Accrued vacation	377	310
Accrued payroll and commission	208	263
Accrued audit and tax services	162	575
Accrued local tax	122	9
Accrued legal costs	117	36
Accrued chargebacks and discounts	68	—
Accrued payroll tax	8	1
Accrued other	2,017	1,482
<b>Total</b>	<b>\$ 3,798</b>	<b>\$ 8,165</b>

Other accrued liabilities as of December 31, 2023 and 2022 largely consist of consultancy fees, contract fees and scientific advisory board fees.

**7. Debt**

Notes payable at December 31, 2023 and 2022 consisted of the following:

	December 31, 2023	December 31, 2022
(in thousands)		
Notes designated at Fair Value Option	\$ 30,943	\$ 7,839
Royalty Interest	5,635	38,931
Insurance Financing	172	235
Tempesta Note	150	250
<b>Total</b>	<b>36,900</b>	<b>47,255</b>
Less: unamortized discount and debt issuance costs	(1,040)	(13,628)
Note payable, net of discount	\$ 35,860	\$ 33,627
Notes payable - non-current, net	\$ 30,993	\$ 17,744
Notes payable - current, net	<b>\$ 4,867</b>	<b>\$ 15,883</b>

Future maturities of the notes payable as of December 31, 2023 are as follows:

	Amounts
(in thousands)	
Periods ended December 31,	
2024	\$ 5,907
2025	50
	5,957
Less: unamortized discount and debt issuance costs	(1,040)
<b>Total</b>	<b>\$ 4,917</b>

Future maturities are based on contractual minimum payments. Timing of maturities may fluctuate based on future revenue.

***Sale of Future Royalty Interest***

***October 2020 Purchase Agreement***

On October 8, 2020, the Company entered into another royalty interest purchase agreement (the "October 2020 Purchase Agreement") with Iliad, pursuant to which the Company sold to Iliad a royalty interest entitling Iliad to receive \$ 12.0 million of future royalties on sales of Mytesi and certain up-front license fees and milestone payments from licensees and/or distributors (the "Royalty Repayment Amount") for an aggregate purchase price of \$ 6.0 million.

Until such time as the Royalty Repayment Amount has been paid in full, the Company will pay Iliad 10 % of the Company's net sales on included products and 10 % of worldwide revenues related to upfront licensing fees and milestone payments from licensees and/or distributors, but specifically excluding licensing fees and/or milestone payments that are reimbursements of clinical trial expenses (the "Royalty Payments"). Beginning on the six-month anniversary of the delivery of the October 2020 Purchase Agreement to the Company (the "Purchase Price Date") and continuing until the 12-month anniversary of the Purchase Price Date, the monthly Royalty Payment shall be the greater of (a) \$ 250,000 , and (b) the actual Royalty Payment amount Iliad is entitled to for such month. Beginning on the 12-month anniversary of the Purchase Price Date and continuing until 18-month anniversary of the Purchase Price Date, the monthly Royalty Payment shall be the greater of (a) \$ 400,000 and (b) the actual Royalty Payment amount Iliad is entitled to for such month. Beginning on the 18-month anniversary of the Purchase Price Date and continuing until 24-month anniversary of the Purchase Price Date, the monthly Royalty Payment shall be the greater of (a) \$ 600,000 and (b) the actual Royalty Payment amount Iliad is entitled to for such month. Beginning on the 24-month anniversary of the Purchase Price Date and continuing until the Royalty Repayment Amount has been paid in full, the

monthly Royalty Payment shall be the greater of (a) \$ 750,000 , and (b) the actual Royalty Payment amount Iliad is entitled to for such month.

The Royalty Interest amount of \$ 12.0 million is classified as debt, net of a \$ 6.0 million discount. Under ASC 470-10-35-3, royalty payments to Iliad will be amortized under the interest method per ASC 835-30. Because there is no set interest rate, and because the royalty payments are variable, the discount rate is variable. After each royalty payment, the Company will use a prospective method to determine a new discount rate based on the revised estimate of remaining cash flows. The new rate is the discount rate that equates the present value of the revised estimate of remaining cash flows with the carrying amount of the debt, and it will be used to recognize interest expense for the remaining periods. At issuance, based on projected cash outflows from future revenue streams, the discount rate was 34.51 %.

Pursuant to the October 2020 Purchase Agreement, if the weekly volume weighted average price ("VWAP") of the Company's common stock is not equal or greater than the minimum VWAP of \$ 0.9105 at least twice during each calendar month during the six-month period beginning on November 1, 2020, then the Royalty Repayment Amount will be automatically increased by \$ 6.0 million at the end of such six-month period. During the observation period starting November 1, 2020, the Company's weekly VWAP failed to reach the minimum VWAP of \$ 0.9105 and on November 13, 2020, the Company concluded that the contingent clause has been met, warranting an additional \$ 6.0 million Royalty Repayment Amount, to be added to the outstanding balance commencing on May 10, 2021 for the purpose of cash interest calculation. The change in the Royalty Repayment Amount was accounted for as a debt modification and resulted in a new discount rate of 45.42 %.

On April 13, 2021, the Company entered into an exchange agreement with Iliad, pursuant to which the parties agreed to partition \$ 3.0 million from the original outstanding balance of the royalty interest. The parties further agreed to exchange the partitioned royalty for 7,843 shares of the Company's common stock. The exchange consisted of Iliad surrendering the partitioned royalty in exchange for the exchange shares. The exchange agreement was accounted for as a modification and resulted in a new discount rate of 77.09 %. As of December 31, 2023, the forecasted future revenues changed which resulted to a new discount rate of 74.59 %.

On February 11, 2022, the Company entered into an exchange agreement with Iliad, pursuant to which the parties agreed to partition \$ 2.4 million from the outstanding balance of the royalty interest. The parties further agreed to exchange the partitioned royalty for 23,117 shares of the Company's common stock. The exchange consisted of Iliad surrendering the partitioned royalty in exchange for the exchange shares.

On March 2, 2022, the Company entered into an exchange agreement with Iliad, pursuant to which the parties agreed to partition \$ 1.1 million from the outstanding balance of the royalty interest. The parties further agreed to exchange the partitioned royalty for 32,333 shares of the Company's common stock. The exchange consisted of Iliad surrendering the partitioned royalty in exchange for the exchange shares.

On March 4, 2022, the Company entered into an exchange agreement with Iliad, pursuant to which the parties agreed to partition \$ 800,000 from the outstanding balance of the royalty interest. The parties further agreed to exchange the partitioned royalty for 26,667 shares of the Company's common stock. The exchange consisted of Iliad surrendering the partitioned royalty in exchange for the exchange shares.

On March 9, 2022, the Company entered into an exchange agreement with Iliad, pursuant to which the parties agreed to partition \$ 700,000 from the outstanding balance of the royalty interest. The parties further agreed to exchange the partitioned royalty for 24,667 shares of the Company's common stock. The exchange consisted of Iliad surrendering the partitioned royalty in exchange for the exchange shares.

Because the period between the first and last exchanges occurred within a 12-month period and each was individually assessed as a modification, the debt terms that existed prior to the February 13 exchange was used in the application of the 10% test on the cumulative assessment performed. The exchanges were cumulatively accounted for as an extinguishment and resulted in a loss of \$ 2.2 million.

On April 14, 2022, the Company entered into amendments (the "Royalty Interest Global Amendments") to its existing royalty interests including the Royalty Interest in the original principal amount of \$ 12.0 million under the October 2020 Royalty Interest. The amendment grants the Company at its sole discretion, the right to exchange from time to time, all or any portion of the Royalty Interests for shares of the Company's common stock at a price per share equal to the Nasdaq Minimum Price (as defined in Nasdaq Listing Rule 5635(d)) as of date of the applicable exchange. Under the Royalty Interest Global Amendments, the Company's ability to exchange the Royalty Interests for shares of the Company's common stock is subject to certain limitations, on which the Company will not have such right and issue any common stock to investors if (a) the issuance of the Company's common shares would cause investor's beneficial ownership to exceed 4.99 % of Company's issued and outstanding common stock as of such date; (b) any of the exchange conditions has not been satisfied as of the applicable exchange date; and (c) the total cumulative number of shares of the Company's common stock issued pursuant to the Royalty Interests would exceed the requirements of The Nasdaq Capital Market (including the rules related to the aggregation of offerings under Nasdaq Listing Rule 5635(d) if applicable) (the "Exchange Cap"), unless stockholder approval is obtained to issue more than the Exchange Cap. The Exchange Cap shall be appropriately adjusted for any reorganization, recapitalization, non-cash dividend, stock split, reverse stock split or other similar transaction.

On May 13, 2022, the Company entered into an exchange agreement with Iliad, pursuant to which the parties agreed to partition \$ 400,000 from the outstanding balance of the royalty interest. The parties further agreed to exchange the partitioned royalty for 15,249 shares of the Company's common stock. The exchange consisted of Iliad surrendering the partitioned royalty in exchange for the exchange shares.

On July 25, 2022, the Company entered into an exchange agreement with Iliad, pursuant to which the parties agreed to partition \$ 750,000 from the outstanding balance of the royalty interest. The parties further agreed to exchange the partitioned royalty for 31,546 shares of the Company's stock. The exchange consisted of Iliad surrendering the partitioned royalty in exchange for the exchange shares.

On November 18, 2022, the Company entered into another exchange agreement with Iliad, pursuant to which the parties agreed to partition \$ 715,000 from the outstanding balance of the royalty interest. The parties further agreed to exchange the partitioned royalty for 73,333 shares of the Company's stock. The exchange consisted of Iliad surrendering the partitioned royalty in exchange for the exchange shares.

On March 17 and 23, 2023, the Company entered into another exchange agreement with Iliad, pursuant to which the parties agreed to partition \$ 992,000 and \$ 227,000 , respectively from the outstanding balance of the royalty interest. The parties further agreed to exchange the partitioned royalty for 14,533 and 3,733 shares, respectively of the Company's stock. The exchange consisted of Iliad surrendering the partitioned royalty in exchange for the exchange shares.

The exchanges that occurred within the 12-month period prior to May 13, 2022 exchange were previously accounted for as extinguishment, therefore, cumulative assessment was not performed anymore.

On May 8, 2023, the Company entered into a standstill agreement (as amended, the "Standstill Agreement") with Iliad, Uptown Capital, LLC (f/k/a Irving Park Capital, LLC) ("Uptown") and Streeterville Capital, LLC ("Streeterville", and together with Iliad and Uptown, collectively, "Investor") to allow the Company to refrain from making royalty payments with respect to four outstanding royalty interests issued by the Company to Investor dated October 8, 2020, December 22, 2020, March 8, 2021, and August 24, 2022, respectively (each, a "Royalty Interest" and collectively, the "Royalty Interests"), including any royalty payments due and payable as of May 8, 2023 (the "Standstill Date"), and refrain from buying, selling, or otherwise trading in the Company's common stock for a period beginning on the Standstill Date and ending on the earliest of (a) the date that is six months following the Standstill Date (b) the date of the public announcement of the probability value in Jaguar's OnTarget Phase 3 clinical trial of crofelemer for prophylaxis of cancer therapy-related diarrhea (c) and the date of any offering or sale of any debt or equity securities, including without limitation any at-the-market offering (the "Standstill Period"), but excluding any exempt issuances. As a material inducement and consideration for Investor's agreement to enter into the Standstill Agreement, the Company issued (i) Iliad warrants to purchase up to 826,738 shares of the common stock, (ii) Uptown

warrants to purchase up to 1,097,756 shares of the common stock, and (iii) Streeterville warrants to purchase up to 1,892,808 shares of the common stock, at an exercise price of \$ 0.48 per share.

On June 28, 2023, the Company entered into the first amendment to the Standstill Agreement, pursuant to which the Standstill Agreement was amended to, among other things, permit (i) the Company to issue an aggregate of 105 shares of the Company's Series H Convertible Preferred Stock to Investor in exchange for a \$ 756,992 reduction in the outstanding balance of the December 2020 Royalty Interest and a \$ 1,726,888 reduction in the outstanding balance of the August 2022 Royalty Interest (the "Exchange Transaction") without triggering the termination of the Standstill Period, and (ii) Investor to (A) consummate the Exchange Transaction during the Standstill Period and (B) sell all shares of the Company's common stock beneficially owned by Investor immediately prior to the consummation of the Exchange Transaction during the Standstill Period.

On June 30, 2023, the Company entered into a binding memorandum of understanding (the "Binding MOU") with the Investor to modify the allocation of the warrants as set forth in the Standstill Agreement such that the Company issued (i) Iliad warrants to purchase up to 1,711,954 shares of the common stock and (ii) Uptown warrants to purchase up to 2,105,348 shares of the common stock, and no warrants were issued to Streeterville under the Standstill Agreement.

On August 14, 2023, the Company entered into an amendment ("the Second Amendment") to the Standstill Agreement with Iliad and Uptown (together, "Standstill Investor") to (i) permit the Company to offer and sell securities without triggering the termination of the Standstill Period, and (ii) remove the restriction on Standstill Investor's ability to buy, sell, or otherwise trade in shares of the Company's common stock during the Standstill Period.

On September 29, 2023, the Company entered into the Global Amendment No. 2 to the October 2020 Royalty Interest with Iliad, pursuant to which, beginning on January 1, 2026, the monthly Royalty Payment under the October 2020 Royalty Interest shall be the greater of (a) \$ 750,000.00 , and (b) the actual Royalty Payment amount Iliad is entitled to for such month pursuant to the terms of the October 2020 Royalty Interest. As a material consideration for Iliad's agreement to enter into this amendment, the Company agreed to issue to Iliad warrants to purchase up to 232,500 shares of the Company's common stock at an exercise price of \$ 0.37 per share. Such warrants may be exercisable for cash or on a cashless basis at any time and from time to time during the period commencing on September 29, 2023 (the "Issuance Date") and ending on the five-year anniversary of the Issuance Date. Pursuant to an analysis of the indicators provided in ASC 470-60-55-8, the Company is not deemed to be experiencing financial difficulty. The debt restructuring is therefore not considered a TDR.

The cumulative effect of the exchanges to the October 2020 Royalty Interest resulted in significant modifications and was accounted for as extinguishment. The Company recorded an extinguishment gain in the audited consolidated statements of comprehensive loss amounting to \$ 2.0 million. The extinguishment triggered a remeasurement event under ASC 825-10 and created an election date on whether to account for the October 2020 Royalty Interest under the fair value option accounting. The Company irrevocably elected to remeasure and subsequently apply the FVO accounting to the entire note. The Company used the valuation report from an independent valuation service provided to measure the reporting date fair value of the note.

On December 28, 2023, the Company entered into a privately negotiated exchange agreement with Iliad, pursuant to which the Company issued an aggregate of 4,875,000 shares of the Company's Common Stocks to Iliad in exchange for a \$ 789,000 reduction in the outstanding balance of the October 2020 Royalty Interest. The effect of the exchange was accounted for as a debt modification.

On December 31, 2023, the fair value was determined to be \$ 6.9 million. For the year ended December 31, 2023, the net loss in the fair value was \$ 1.1 million. The net loss in fair value was recorded in the change in fair value of freestanding and hybrid financial instruments designated at FVO in the audited consolidated statements of comprehensive loss.

*December 2020 Purchase Agreement*

On December 22, 2020, the Company entered into a royalty interest purchase agreement (the "December 2020 Purchase Agreement") with Irving Park Capital, LLC ("Uptown"), pursuant to which the Company sold to Irving a royalty interest entitling Irving to receive \$ 12.0 million of future royalties on sales of Mytesi and certain up-front license fees and milestone payments from licensees and/or distributors (the "Royalty Repayment Amount") for an aggregate purchase price of \$ 6.0 million.

Until such time as the Royalty Repayment Amount has been paid in full, the Company will pay Uptown 10 % of the Company's Net Sales on Included Products and 10 % of worldwide revenues related to upfront licensing fees and milestone payments from licensees and/or distributors, but specifically excluding licensing fees and/or milestone payments that are reimbursements of clinical trial expenses (the "Royalty Payments"). Beginning on the payment start date and continuing until the 12-month anniversary of the Purchase Price Date, the monthly Royalty Payment shall be the greater of (a) \$ 750,000 , and (b) the actual Royalty Payment amount Irving is entitled to for such month.

The December 2020 Royalty Interest amount of \$ 12.0 million is classified as debt, net of a \$ 6.0 million discount, at initial recognition. Under ASC 470-10-35-3, royalty payments to Uptown will be amortized under the interest method per ASC 835-30. Because there is no set interest rate, and because the royalty payments are variable, the discount rate is variable. After each royalty payment, the Company will use a prospective method to determine a new discount rate based on the revised estimate of remaining cash flows. The new rate is the discount rate that equates the present value of the revised estimate of remaining cash flows with the carrying amount of the debt, and it will be used to recognize interest expense for the remaining periods. At issuance, based on projected cash outflows from future revenue streams, the discount rate was 23.70 %.

On April 14, 2022, under the Royalty Interest Global Amendments, the Company is granted at its sole discretion, the right to exchange from time to time, all or any of the Royalty Interest under the original principal amount of \$ 12.0 million or any portion of the December 2020 Purchase Agreement for shares of the Company's common stock at a price per share equal to the Nasdaq Minimum Price (as defined in Nasdaq Listing Rule 5635(d)) as of date of the applicable exchange, subject to certain limitations.

On May 8, 2023, the Company entered into an exchange agreement with Uptown to (i) partition a new royalty interest in the royalty repayment amount of \$ 1,073,807 from the outstanding balance of the royalty interest. The parties further agreed to exchange the partitioned royalty for 1,908,651 shares of the Company's common stock.

On the same date, the Company entered into the Standstill Agreement as described further above, pursuant to which the Company may refrain from making royalty payments on the December 2020 Royalty Interest during the Standstill Period.

On September 29, 2023, the Company entered into the Global Amendment No. 2 to the December 2020 Royalty Interest with Uptown, pursuant to which, beginning on January 1, 2026, the monthly Royalty Payment under the December 2020 Royalty Interest shall be the greater of (a) \$ 750,000.00 , and (b) the actual Royalty Payment amount Uptown is entitled to for such month pursuant to the terms of the December 2020 Royalty Interest. As a material consideration for Uptown's agreement to enter into this amendment, the Company agreed to issue to Uptown warrants to purchase up to 262,500 shares of the Company's common stock at an exercise price of \$ 0.37 per share. Such warrants may be exercisable for cash or on a cashless basis at any time and from time to time during the period commencing on September 29, 2023 (the "Issuance Date") and ending on the five-year anniversary of the Issuance Date. Pursuant to an analysis of the indicators provided in ASC 470-60-55-8, the Company is not deemed to be experiencing financial difficulty. The debt restructuring is therefore not considered a TDR.

On the same date, the Company entered into a privately negotiated exchange agreement with Uptown (the "Exchange Agreement"), pursuant to which the Company issued an aggregate of 118 shares of the Company's newly authorized Series I Convertible Preferred Stock (the "Series I Preferred Stock" or "Preferred Stock") to Uptown, at an effective exchange price per share equal to the market price (defined as the Minimum Price under Nasdaq Listing

Rule 5635(d)) as of the date of the Exchange Agreement, in exchange for a \$ 1,500,000.00 reduction in the outstanding balance of the December 2020 Royalty Interest ("Partitioned Royalty").(the "Exchange Transaction"). Subject to the terms of the Series I Preferred Stock, each share of Series I Preferred Stock is convertible into shares of the Company's Common Stock (the "Conversion Shares").

The cumulative effect of the exchanges to the December 2020 Purchase Agreement resulted in significant modifications and was accounted for as extinguishment. The Company recorded an extinguishment gain in the audited consolidated statements of comprehensive loss amounting to \$ 2.7 million. The extinguishment triggered a remeasurement event under ASC 825-10 and created an election date on whether to account for the December 2020 Purchase Agreement under the FVO accounting.

The Company irrevocably elected to initially and subsequently apply the FVO accounting to the entire note. The Company used the valuation report from an independent valuation service provided to measure the reporting date fair value of the note. On December 31, 2023, the fair value was determined to be \$ 7.5 million. For the year ended December 31, 2023, the net loss in the fair value was \$ 1.4 million. The net loss in fair value was recorded in the change in fair value of freestanding and hybrid financial instruments designated at FVO in the audited consolidated statements of comprehensive loss.

*March 2021 Purchase Agreement*

On March 8, 2021, the Company entered into a purchase agreement (the "March 2021 Purchase Agreement") with Streeterville Capital, LLC ("Streeterville"), a company affiliated with CVP, pursuant to which the Company sold a royalty interest entitling Streeterville to \$ 10.0 million and any interest, fees, and charges as royalty repayment amount for an aggregate purchase price of \$ 5.0 million. Interest will accrue on the royalty repayment amount at a rate of 5 % per annum, compounding quarterly, and will increase to 10 % per annum, compounding quarterly on the 12-month anniversary of the closing date.

The Company will be obligated to make minimum royalty payments on a monthly basis beginning at the earlier of (a) 36 months following the closing date or (b) 30 days following the satisfaction of all existing royalties to Streeterville, and its affiliates namely Iliad and Irving, but not earlier than 18 months following the closing date in an amount equal to the greater of (i) \$ 250,000 beginning on the royalty payment start date and continuing until either the royalty repayment amount has been paid in full or the 6-month anniversary of the royalty payment start date, \$ 400,000 beginning on the 6-month anniversary of the royalty payment start date and continuing until either the royalty repayment amount has been paid in full or the 12-month anniversary of the royalty payment start date, \$ 600,000 beginning on the 12-month anniversary of the royalty payment start date and continuing until either the royalty repayment amount has been paid in full or the 18-month anniversary of the royalty payment start date, \$ 750,000 beginning on the 18-month anniversary of the royalty payment start date and continuing until the royalty repayment amount has been paid in full, and (ii) 10 % of the Company's net sales on included products, 10 % of worldwide revenues related to upfront licensing fees and milestone payments from licensees and/or distributors but specifically excluding licensing fees and/or milestone payments that are reimbursements of clinical trial expenses or associated with the license of Included Products from the Company to Napo Therapeutics, including but not limited to the upfront fee payable by Napo Therapeutics to Napo for included products and Crofelemer for other indications; and 50 % of royalties collected from licenses of the included products to third parties.

The March 2021 Royalty Interest amount of \$ 10.0 million is classified as debt, net of a \$ 5.0 million discount, at initial recognition. Under ASC 470-10-35-3, royalty payments to Streeterville will be amortized under the interest method per ASC 835-30. Because there is no set interest rate, and because the royalty payments are variable, the discount rate is variable. After each royalty payment, the Company will use a prospective method to determine a new discount rate based on the revised estimate of remaining cash flows. The new rate is the discount rate that equates the present value of the revised estimate of remaining cash flows with the carrying amount of the debt, and it will be used to recognize interest expense for the remaining periods. At issuance, based on projected cash outflows from future revenue streams, the discount rate was 19.36 %.

On April 14, 2022, under the Royalty Interest Global Amendments, the Company is granted at its sole discretion, the right to exchange from time to time, all or any of the Royalty Interest under the original principal amount of \$ 10.0 million of the March 2021 Purchase Agreement for shares of the Company's common stock at a price per share equal to the Nasdaq Minimum Price (as defined in Nasdaq Listing Rule 5635(d)) as of date of the applicable exchange, subject to certain limitations.

On August 17, 2022, the Company entered into an exchange agreement (the "Royalty Interest Exchange Agreement") with Streeterville to (i) partition a new royalty interest in the royalty repayment amount of \$ 3.4 million ("Partitioned Royalty") from the royalty interest of the March 2021 Purchase Agreement and then cause the outstanding balance of the royalty interest to be reduced by an amount equal to the initial outstanding balance of the Partitioned Royalty, and (ii) exchange ("Royalty Exchange") the Partitioned Royalty for 153,333 million shares of the Company's common stock with a par value of \$ 0.0001 in accordance with the term of the Royalty Interest Exchange Agreement. Under the terms of the Royalty Interest Exchange Agreement, the Royalty Exchange will consist of Streeterville surrendering the Partitioned Royalty in exchange for the shares, free of any restrictive securities legend, and Streeterville shall give no consideration of any kind whatsoever to the Company in connection with the Royalty Interest Exchange Agreement.

On September 30, 2022, the Company entered into an exchange agreement with Streeterville, pursuant to which the parties agreed to partition \$ 2.0 million from the outstanding balance of the royalty interest. The parties further agreed to exchange the partitioned royalty for 156,863 shares of the Company's common stock. The exchange consisted of Streeterville surrendering the partitioned royalty in exchange for the exchange shares. The exchange was accounted for as a debt modification and resulted to a reduction in the outstanding balance of the royalty interest amounting to \$ 2.0 million.

As of December 31, 2023 the forecasted future revenues changed which resulted to a new discount of 53.85 %.

Interest expense for the years ended December 31, 2023 and 2022 was \$ 2.1 million and \$ 1.9 million, respectively. As of December 31, 2023 and 2022, the carrying value of the debt was \$ 4.6 million and \$ 3.1 million, respectively.

*August 2022 Purchase Agreement*

On August 24, 2022, the Company entered into another royalty interest purchase agreement (the "August 2022 Purchase Agreement") with Streeterville, pursuant to which the Company sold to Streeterville (the entitled "Investor") a royalty interest to receive \$ 12.0 million of future royalties on sales of Mytesi® (crofelemer) for any indications that could cannibalize crofelemer indications or any other chronic indication and certain up-front license fees and milestone payments from licensees and/or distributors for an aggregate purchase price of \$ 4.0 million ("the Royalty Financing"). The Company will use the proceeds to support the ongoing pivotal phase 3 clinical trial of crofelemer for prophylaxis of diarrhea in adults receiving targeted cancer therapy. Interest will accrue on the Royalty Repayment Amount at a rate of 5 % per annum from the closing of the Royalty Financing until the one-year anniversary of such closing and 10 % per annum thereafter, simple interest computed on the basis of a 360-day year comprised of twelve 30-day months.

The Company will be obligated to make minimum royalty payments on a monthly basis beginning on January 1, 2024 in an amount equal to the greater of (A) \$ 250,000 (which increases to \$ 400,000 beginning 6 months following the closing of the Royalty Financing, \$ 600,000 beginning 12 months following the closing of the Royalty Financing, and \$ 750,000 beginning 18 months following the closing of the Royalty Financing) and (B) the royalty payments to which Investor is entitled, consisting of (1) 10 % of the Company's net sales of crofelemer for any indications that could cannibalize crofelemer indications or any other chronic indication (including any improvements, modifications and follow-on products, collectively referred to as "Included Products") (2) 10 % of worldwide revenues related to upfront licensing fees and milestone payments from licensees and/or distributors, but specifically excluding licensing fees and/or milestone payments that are (A) reimbursements of clinical trial expenses or (B) associated with

the license of the of the Included Products from the Company to Napo EU S.p.A. and (3) 50 % of royalties collected from licenses of the Included Products to third parties.

Pursuant to the terms of the Royalty Interest, the Company has the right to exchange from time to time at the Company's sole discretion all or any portion of the Royalty Interest for shares of Common Stock at a price per share equal to the Nasdaq Minimum Price (as defined in Nasdaq Listing Rule 5635(d)) as of the date of the applicable exchange. At issuance, based on projected cash outflows from future revenue streams, the discount rate was 55.97 %.

On September 29, 2023, the Company entered into a Global Amendment No. 2 (the "Global Amendment") with the Investor as described further above, such that the Company issued Streeterville warrants to purchase 255,000 shares of the common stock the Global Amendment No. 1 and Global Amendment No. 2 to the August 2022 Royalty Interest with Streeterville, pursuant to which, (a) beginning on January 1, 2026, the monthly Royalty Payment under the August 2022 Royalty Interest shall be the greater of (x) \$ 750,000.00 , and (y) the actual Royalty Payment amount Streeterville is entitled to for such month pursuant to the terms of the August 2022 Royalty Interest, and (b) the Company is prohibited from making prepayments of the Royalty Repayment Amount under the August 2022 Royalty Interest. As a material consideration for Streeterville's agreement to enter into these amendments, the Company agreed to issue to Streeterville warrants to purchase up to 255,000 shares of the Company's common stock at an exercise price of \$ 0.37 per share. Such warrants may be exercisable for cash or on a cashless basis at any time and from time to time during the period commencing on September 29, 2023 (the "Issuance Date") and ending on the five-year anniversary of the Issuance Date. Pursuant to an analysis of the indicators provided in ASC 470-60-55-8, the Company is not deemed to be experiencing financial difficulty. The debt restructuring is therefore not considered a TDR.

The cumulative effect of the exchanges to the August 2022 Purchase Agreement resulted to significant modifications and were accounted for as extinguishment. The Company recorded an extinguishment loss in the audited consolidated statements of comprehensive loss amounting to \$ 1.0 million. The extinguishment triggered a remeasurement event under ASC 825-10 and created an election date on whether to account for the August 2022 Purchase Agreement resulted under the FVO accounting.

The Company irrevocably elected to initially and subsequently apply the FVO accounting to the entire note. The Company used the valuation report from an independent valuation service provided to measure the reporting date fair value of the note. On December 31, 2023, the fair value was determined to be \$ 6.8 million. For the year ended December 31, 2023, the net loss in the fair value was \$ 661,000 . The net loss in fair value was recorded in the change in fair value of freestanding and hybrid financial instruments designated at FVO in the audited consolidated statements of comprehensive loss.

#### **Streeterville Note**

On January 13, 2021, the Company issued a secured promissory note to Streeterville in the original principal amount of \$ 6.2 million for an aggregate purchase price of \$ 6.0 million. The Company will use the proceeds to fund development of the Company's NP-300 drug product candidate for the indication of the symptomatic relief of diarrhea from cholera and general corporate purposes, including the Company's product pipeline activities. The note is due after four years and bears interest at 3.25 % per annum. Interest on the note is payable annually in advance by adding the interest charge for each upcoming year to the outstanding balance on the date each such interest charge is accrued. The Company also paid \$ 25,000 to cover legal fees, accounting costs, due diligence, monitoring and other transaction costs incurred in connection with the issuance of the note. The first year of prepaid interest and the transaction expenses are included in the original principal amount.

At any time following the occurrence of a trial failure which refers to any of the following: (i) the Company abandons the clinical trial with NP-300 for an indication for the symptomatic relief of infectious diarrhea for cholera; (ii) the Company fails to start the Phase 1 clinical trial of NP-300 for the symptomatic relief of infectious diarrhea for cholera by July 1, 2022; or (iii) the Company fails to meet all primary endpoints in the pivotal trials of NP-300 for the symptomatic relief of infectious diarrhea for cholera with statistical significance, Streeterville may elect to increase the outstanding balance as of the date of the trial failure by 25 % without acceleration (the "Trial Failure Effect"). If

Streeterville elects to apply the Trial Failure Effect, it reserves the right to declare the outstanding balance immediately due and payable at any time. As of December 31, 2022, no trial failure occurred.

Streeterville is entitled to a maximum of 18 % and a minimum of 1 % of the gross proceeds received by the Company from the sale of TDPRV (the "Return Bonus"). The Return Bonus percentage is reduced pro rata based on the percentage of the original principal balance of the note that has been repaid as of the date of the sale of the TDPRV. Even if the note has been paid in full at the time of the sale of the TDPRV, the Company is still obliged to pay Streeterville a Return Bonus of 1 %. If Streeterville applies the Trial Failure Effect, the Return Bonus will automatically be reduced to 1 %. If the TDPRV has not been sold as of the day immediately preceding the maturity date of the note, the Return Bonus percentage will be fixed as of such date. As of December 31, 2022, the Company has not sold any TDPRV.

Beginning on the earlier of (a) 6 months after January 2021, and (b) initiation of human trials with NP-300 for symptomatic relief of infectious diarrhea for cholera, the Company may pay all or any portion of the outstanding balance earlier than it is due. In the event the Company elects to prepay all or any portion of the outstanding balance, it shall pay to Streeterville 112.5 % of the portion of the outstanding balance the Company elects to prepay. The Company may not prepay the note without the Streeterville's consent on the date the last patient is enrolled in a pivotal trial.

After Streeterville becomes aware of the occurrence of any default, Streeterville may accelerate the note, with the outstanding balance becoming immediately due and payable in cash at the Mandatory Default Amount (i.e., the outstanding balance following the application of the Default Effect). Streeterville reserves the right to declare the outstanding balance immediately due and payable at any time following the default. Default Effect means multiplying the outstanding balance as of the date of default by 5 % or 15 % for each occurrence of default, capped at an aggregate of 25 %, and then adding the resulting product to the outstanding balance. The percentage to be used depends on whether the default is viewed as minor or major as defined in the agreement. Furthermore, interest accrues on the outstanding balance beginning on the date of default at an interest rate equal to the lesser of 18 % per annum or the maximum rate permitted under applicable law. As of December 31, 2023, no default has occurred.

In connection with the note issuance, the Company has entered into a security agreement with Streeterville, pursuant to which Streeterville will receive a first priority security interest in all existing and future NP-300 technology, and any TDPRV and the sale proceeds therefrom that may be granted to the Company by the FDA in connection with the development of NP-300 for the cholera-related indication. The Company also agreed, with certain exceptions, not to grant any lien on any of the collateral securing the note and not to grant any license under any of the intellectual property relating to such collateral. The grant of security interest has become effective upon the receipt of the Salix Waiver on April 6, 2021 in observance to the requirement of the settlement agreement previously entered by the Company with Salix Pharmaceuticals, Inc.

The Company irrevocably elected to initially and subsequently apply the FVO accounting to the entire note. The fair value at the transaction date was equal to the cash proceeds received of \$ 6.0 million. The transaction expense of \$ 25,000 was recognized in profit and loss as incurred. The Company used the valuation report from an independent valuation service provided to measure the reporting date fair value of the note. At December 31, 2023 and 2022, the fair values were determined to be \$ 9.8 million and \$ 7.8 million, respectively. For the year ended December 31, 2023 and 2022, the net losses in the fair value of \$ 2.0 million and \$ 20,000 , respectively were recorded in the change in fair value of freestanding and hybrid financial instruments designated at FVO in the consolidated statements of operations.

#### ***Insurance Financing***

##### ***March 2022 First Insurance Financing***

In March 2022, the Company entered into a premium finance agreement for \$ 100,000 with First Insurance Funding ("First Insurance") representing the unpaid balance of the total premiums, taxes, and fees of \$ 115,000 with an annual interest rate of 4.6 %. The total finance charge was \$ 15,000 . Payment of principal and interest is due in equal monthly installments over ten months . The Company granted and assigned First Insurance a first priority lien on

and security interest in the financed policies and any additional premium required under the financed policies. Interest expense for the year ended December 31, 2023 and 2022 was zero. The financing balance was zero and \$ 9,000 at December 31, 2023 and 2022, respectively.

*May 2022 First Insurance Financing*

In May 2022, the Company entered into another premium finance agreement for \$ 752,000 with First Insurance representing the unpaid balance of the total premiums, taxes, and fees of \$ 941,000 with an annual interest rate of 4.3 %. The total finance charge was \$ 15,000 . Payment of principal and interest is due in equal monthly installments over ten months . Interest expense for the year ended December 31, 2023 and 2022 was zero . The financing balance was zero and \$ 226,000 at December 31, 2023 and 2022, respectively.

*March 2023 First Insurance Financing*

In March 2023, the Company entered into another premium finance agreement for \$ 98,000 with First Insurance representing the unpaid balance of the total premiums, taxes, and fees of \$ 115,000 with an annual interest rate of 8.6 %. The total finance charge was \$ 2,000 . Payment of principal and interest is due in equal monthly installments over ten months . Interest expense for year ended December 31, 2023 \$ 33,000 . The financing balance was zero as of December 31, 2023.

*May 2023 First Insurance Financing*

In May 2023, the Company entered into another premium finance agreement for \$ 575,000 with First Insurance representing the unpaid balance of the total premiums, taxes, and fees of \$ 676,000 with an annual interest rate of 8.6 %. The total finance charge was \$ 23,000 . Payment of principal and interest is due in equal monthly installments over ten months . Interest expense for the year ended December 31, 2023, was \$ 16,000 . The financing balance was \$ 172,000 as of December 31, 2023.

**2019 Tempesta Note**

In October 2019, the Company entered into a License Termination and Settlement Agreement with Dr. Michael Tempesta ("Tempesta"), pursuant to which certain royalty payment disputes between Napo and Tempesta were settled. Per the terms of the Agreement, Tempesta received \$ 50,000 in cash, an unsecured promissory note issued by the Company in the aggregate principal amount of \$ 550,000 and 178 shares of the Company's common stock in exchange for the cessation of all royalty payments by Napo to Dr. Tempesta under the License Agreements. The \$ 550,000 promissory note bears interest at the rate of 2.5 % per annum and matures on March 1, 2025. The promissory note provides for the Company to make semiannual payments equal to \$ 50,000 plus accrued interest beginning on March 1, 2020 until the note is paid in full. Interest expense for the years ended December 31, 2023 and 2022 was \$ 5,000 and \$ 10,000 , respectively. At December 31, 2023 and 2022, the net carrying value of the Tempesta note was \$ 150,000 and \$ 250,000 respectively.

## 8. Warrants

The following table summarizes information about warrants outstanding and exercisable into shares of the Company's common stock for the years ended December 31, 2023 and 2022:

	December 31, 2023	December 31, 2022
Warrants outstanding, beginning balance	7,505	7,513
Issuances	11,417,302	—
Exercises	—	—
Expirations and cancelations	—	( 8 )
Warrants outstanding, ending balance	<u>11,424,807</u>	<u>7,505</u>

As of December 31, 2023 and 2022, the Company's outstanding warrants have an exercise price ranging from \$ 0.24 to \$ 1.47 per common share and generally expires prior to December 31, 2024.

### **PIPE Warrants**

On May 8, 2023, the Company entered into a Securities Purchase Agreement (the "PIPE Purchase Agreement") with certain investors named therein (collectively the "Purchasers"), pursuant to which the Company agreed to issue and sell to the Purchasers in a private placement an aggregate of (i) 137 shares (the "Preferred Shares") of Series G Convertible Preferred Stock, par value \$ 0.0001 per share, of the Company ("Series G Preferred Stock") and (ii) warrants to purchase up to 6,850,000 shares of the Company's common stock, at an exercise price of \$ 0.48 per share (the "PIPE Warrants"), for an aggregate purchase price of approximately \$ 1.86 million (the "Private Placement"). The Company intends to use the proceeds from the Private Placement for working capital and general corporate purposes.

The PIPE Warrants may be exercisable for cash or on a cashless basis at any time and from time to time during the period commencing on the later of (i) January 1, 2024, and (ii) the date on which the approval by the Company's stockholders (the "Stockholder Approval") to remove both the Voting Cap and the Conversion Cap (both as defined below) is obtained (the "PIPE Warrants Initial Exercise Date") and ending on the five-year anniversary of the PIPE Warrants Initial Exercise Date.

On May 10, 2023, the Company issued warrants equivalent to 6,850,000 shares of the Company's common stock in relation to the PIPE Purchase Agreement.

The PIPE Purchase Agreement provides that during the period commencing on the signing of the PIPE Purchase Agreement and ending October 22, 2023, the Company will not effect or enter into any agreement to (i) issue securities in exchange for any securities of the Company issued and outstanding on the date of the PIPE Purchase Agreement pursuant to Section 3(a)(9) of the Securities Act of 1933, as amended (the "Securities Act"), or (ii) effect issuance by the Company of common stock or Common Stock Equivalents (as defined in the PIPE Purchase Agreement), subject to certain customary exceptions set forth in the PIPE Purchase Agreement including, among others, issuance of shares of common stock pursuant to the At The Market Offering Agreement, dated December 10, 2021, by and between the Company and Ladenburg Thalmann & Co. Inc., as amended (the "Ladenburg Thalmann ATM"), provided that such issuance in the Ladenburg Thalmann ATM has consented.

On August 14, 2023, the Company entered into an amendment ("the First Amendment") to the PIPE Purchase Agreement with certain holders (the "Holders") named in the PIPE Purchase Agreement, pursuant to which the parties agreed to terminate the restriction on subsequent equity sales by the Company. In exchange for the Holders' agreement to enter into the First Amendment, the Company agreed to issue the Holders warrants to purchase 685,000 shares of the Company's common stock (the "PIPE Amendment Warrants") in a private placement pursuant to Section 4(a)(2) of the Securities Act. The PIPE Amendment Warrants are substantially the same as the PIPE

Warrants and have an exercise price of \$ 0.48 per share. The PIPE Amendment Warrants may be exercisable for cash or on a cashless basis at any time and from time to time during the period commencing on January 1, 2024 (the "PIPE Amendment Warrants Initial Exercise Date") and ending on the fifth anniversary of the PIPE Amendment Warrants Initial Exercise Date.

At the date of the PIPE Amendment Warrants, the warrants were valued at \$ 1.2 million using the Black-Scholes option pricing model as follows: exercise price of \$ 0.48 per share, stock price of \$ 0.72 per share, expected life of five years, volatility of 145.95 % and a risk-free rate of 3.37 %. The warrants were classified in additional paid-in-capital.

***Standstill Agreement***

Pursuant to the Company's entry in the Standstill Agreement, as amended by the Binding MOU, as described further above, the Company agreed to issue (i) Iliad warrants to purchase up to 1,711,954 shares of the common stock, and (ii) Uptown warrants to purchase up to 2,105,348 shares of the common share, at an exercise price of \$ 0.48 per share (the "Standstill Warrants").

The Standstill Warrants may be exercisable for cash or on a cashless basis at any time and from time to time during the period commencing on the later of (i) January 1, 2024 and (ii) the date on which the Stockholder Approval is obtained (the "Standstill Warrant Initial Exercise Date") and ending on the fifth anniversary of the Standstill Warrant Initial Exercise Date.

At the date of the Standstill Agreement, the warrants were valued at \$ 2.5 million using the Black-Scholes option pricing model as follows: exercise price of \$ 0.48 per share, stock price of \$ 0.73 per share, expected life of five years, volatility of 118.88 % and a risk-free rate of 3.49 %. The warrants were classified in additional paid-in-capital.

***Royalty Interest Global Amendments***

On September 29, 2023, the Company entered into amendments (the "Royalty Interest Global Amendments") to (i) the October 2020 Royalty Interest with Iliad, (ii) the December 2020 Royalty Interest with Uptown, and (iii) the August 2022 Royalty Interest with Streeterville, pursuant to which, among other things, the Company agreed to issue to (i) Iliad warrants to purchase up to 232,500 shares of the Company's common stock, (ii) Uptown warrants to purchase up to 262,500 shares of the common stock, and (iii) Streeterville warrants to purchase up to 255,000 shares of the Common Stock, at an exercise price of \$ 0.37 per share (collectively, the "Royalty Interest Global Amendment Warrants").

The Royalty Interest Global Amendment Warrants may be exercisable for cash or on a cashless basis at any time and from time to time during the period commencing on September 29, 2023 (the "Royalty Interest Global Amendment Initial Exercise Date") and ending on the five-year anniversary of the Royalty Interest Global Amendment Initial Exercise Date.

At the date the Royalty Interest Global Amendments, the warrants were valued at \$ 173,000 using the Black-Scholes option pricing model as follows: exercise price of \$ 0.37 per share, stock price of \$ 0.26 per share, expected life of five years, volatility of 139.53 % and a risk-free rate of 4.6 %. The warrants were classified in additional paid-in-capital.

## 9. Preferred Stock

At December 31, 2023 and 2022, preferred stock consisted of the following:

December 31, 2023					
(in thousands, except share and per share data)	Shares Designated	Issued and Outstanding	Carrying Value	Liquidation Preference per Share	
<b>Series</b>					
A	5,524,926	—	\$ —	\$ —	—
B	11,000	—	—	—	—
B-1	63	—	—	—	—
B-2	10,165	—	—	—	—
C	1,011,000	—	—	—	—
D	977,300	—	—	—	—
E	10	—	—	—	—
F	10	—	—	—	—
G	137	122	—	—	—
H	105	—	—	—	—
I	118	56	—	—	—
<b>Total</b>	<b>7,534,834</b>	<b>178</b>	<b>\$ —</b>	<b>\$ —</b>	

December 31, 2022					
(in thousands, except share and per share data)	Shares Designated	Issued and Outstanding	Carrying Value	Liquidation Preference per Share	
<b>Series</b>					
A	5,524,926	—	\$ —	\$ —	—
B	11,000	—	—	—	—
B-1	63	—	—	—	—
B-2	10,165	—	—	—	—
C	1,011,000	—	—	—	—
D	977,300	—	—	—	—
E	10	—	—	—	—
F	10	—	—	—	—
<b>Total</b>	<b>7,534,474</b>	<b>—</b>	<b>\$ —</b>	<b>\$ —</b>	

The Company is authorized to issue a total of 10,000,000 shares of its preferred stock as of December 31, 2023, and December 31, 2022 with a total of 7,534,834 shares and 7,534,474 shares designated to specific Series as of December 31, 2023 and December 31, 2022, respectively.

### Series E Preferred Stock

On August 18, 2022, the Company entered into an agreement (the "Securities Purchase Agreement") with Synworld to issue 10 Series E Preferred Stock with a par value of \$ 0.0001 , amounting to \$ 100 . In consideration of the Securities Purchase Agreement, the Company and Synworld agree to amend the existing definition of the term "Service Share Amount" in the License Agreement entered by both parties and include a subsection for lock-up wherein Synworld agrees not to sell, transfer, loan, grant any option of the purchase of, or otherwise dispose of any shares of common stock acquired pursuant to the License Agreement until after the 90-day period following the date of acquisition.

On October 4, 2022, the Company redeemed all 10 shares of Series E Preferred Stock in accordance with the terms of such securities. As a result, no shares of Series E Preferred Stock remain outstanding.

*Series F Preferred Stock*

On November 11, 2022, the Company entered into an agreement (the "Securities Purchase Agreement") with a third party to issue 10 Series F Preferred Stock with a par value of \$ 0.0001 , amounting to \$ 100 . In consideration of the Securities Purchase Agreement, the Company and third party agree to amend the existing definition of the term "Service Share Amount" in the License Agreement entered by both parties and include a subsection for lock-up wherein the third party agrees not to sell, transfer, loan, grant any option of the purchase of, or otherwise dispose of any shares of common stock acquired pursuant to the License Agreement until after the 90-day period following the date of acquisition.

*Series G Preferred Stock*

On May 8, 2023, the Company entered into a securities purchase agreement with certain investors, pursuant to which the Company agreed to issue to such investors (i) 137 shares of Series G Convertible Preferred Stock, par value \$ 0.0001 per share, of the Company ("Series G Preferred Stock") and (ii) warrants to purchase up to 6,850,000 shares of the Company's common stock, at an exercise price of \$ 0.48 per share (the "PIPE Warrants"), for an aggregate purchase price of approximately \$ 1.9 million (the "Private Placement").

On December 28, 2023, the Company converted 15 shares of Series G Preferred Stock in accordance with the terms of such securities. As a result, 122 shares of Series G Preferred Stock remain outstanding.

*Series H Preferred Stock*

On June 28, 2023, the Company entered into privately negotiated exchange agreements with Uptown and Streeterville, under which the Company issued 32 and 73 shares of the Company's newly authorized Series H Convertible Preferred Stock (the "Series H Preferred Stock") to Uptown and Streeterville, respectively, at an effective exchange price per share equal to the market price (defined as the Minimum Price under Nasdaq Listing Rule 5635(d)) as of the date of the exchange agreements, in exchange for a \$ 757,000 reduction in the outstanding balance of the December 2020 Royalty Interest and a \$ 1.7 million reduction in the outstanding balance of the August 2022 Royalty Interest, respectively. As of December 31, 2023, the company converted all issued shares of Series H and no shares remain outstanding.

*Series I Preferred Stock*

On September 29, 2023, the Company entered into a privately negotiated exchange agreement with Uptown (the "Exchange Agreement"), pursuant to which the Company issued an aggregate of 118 shares of the Company's newly authorized Series I Convertible Preferred Stock (the "Series I Preferred Stock") to Uptown, at an effective exchange price per share equal to the market price (defined as the Minimum Price under Nasdaq Listing Rule 5635(d)) as of the date of the Exchange Agreement, in exchange for a \$ 1.5 million reduction in the outstanding balance of the December 2020 Royalty Interest.

On November 14, 2023, the Company converted 62 shares of Series I Preferred Stock in accordance with the terms of such securities. As a result, 56 shares of Series I Preferred Stock remain outstanding.

## 10. Stockholders' Equity

As of December 31, 2023 and 2022, the Company had reserved shares of common stock, on an as-if converted basis, for issuance as follows:

	December 31, 2023	December 31, 2022
Options issued and outstanding	26,262	26,533
Inducement options issued and outstanding	1,512	1,546
Options available for grant under stock option plans	626,342	122,978
Restricted stock unit awards issued and outstanding	2,708,136	44,865
Warrants issued and outstanding	11,424,807	7,505
<b>Total</b>	<b>14,787,059</b>	<b>203,427</b>

### **Common Stock**

The holders of common stock are entitled to one vote for each share of common stock held. The common stockholders are also entitled to receive dividends whenever funds and assets are legally available and when declared by the Board of Directors.

The holders of non-voting common stock are not entitled to vote, except on an as converted basis with respect to any change of control of the Company that is submitted to the stockholders of the Company for approval. Shares of the Company's non-voting common stock have the same rights to dividends and other distributions and are convertible into shares of the Company's common stock on a one -for-one basis.

At a special meeting of stockholders of Jaguar Health, Inc. (the "Company") held on September 30, 2022 (the "Special Meeting"), the Company's stockholders approved an amendment (the "Sixth Amendment") to the Company's Third Amended and Restated Certificate of Incorporation (the "COI") to effect an increase in the number of authorized shares of the Company's voting common stock, par value \$ 0.0001 per share (the "Common Stock"), from 150,000,000 to 298,000,000 shares of Common Stock (the "Authorized Share Increase") on September 30, 2022.

Pursuant to such authority granted by the Company's stockholders, the Company's board of directors approved the Authorized Share Increase and the filing of the Sixth Amendment to effectuate the Authorized Share Increase. On September 30, 2022, the Company filed the Sixth Amendment with the Secretary of State of the State of Delaware (the "DE Secretary of State"), and the Authorized Share Increase became effective in accordance with the terms of the Sixth Amendment immediately upon filing with the DE Secretary of State (the "Effective Time").

The Company is now authorized to issue a total number of 352,475,074 shares, of which 298,000,000 shares are common stock, 50,000,000 are non-voting common stock and 4,464,011 are preferred stock.

### **Reverse Stock-Split**

On September 3, 2021, the Company filed an amendment to its Third Amended and Restated Certificate of Incorporation with the Secretary of State of Delaware to effect a 1-for-3 reverse stock split of the Company's issued and outstanding shares of voting common stock, effective September 8, 2021. Upon effectivity, every three shares of the Company's issued and outstanding common stock immediately prior to the effective time shall automatically be reclassified into one share of common stock without any change in the par value.

On January 20, 2023, the Company approved another amendment to the Company's Third Amendment and Restated Certificate of Incorporation to effect a 1-for-75 reverse stock split of the Company's issued and outstanding shares of voting common stock, effective January 23, 2023. Upon effectivity, every seventy-five shares of the

Company's issued outstanding common stock immediately prior to the effective time shall automatically be reclassified into one share of common stock without any change in the par value.

The reverse stock splits reduces the number of shares of common stock issuable upon the conversion of the Company's outstanding non-voting common stock and the exercise or vesting of its outstanding stock options and warrants in proportion to the ratio of the reverse stock split and causes a proportionate increase in the conversion and exercise prices of such non-voting common stock, stock options and warrants. In addition, the number of shares reserved for issuance under the Company's equity compensation plans immediately prior to the effective time will be reduced proportionately. The reverse stock split did not change the total number of authorized shares of common stock or preferred stock.

***At The Market Offering ("ATM")***

*December 2021 ATM Agreement*

On December 10, 2021, the Company entered into an ATM Agreement ("December 2021 ATM Agreement") with Ladenburg, pursuant to which the Company may offer and sell, from time to time through Ladenburg, shares of common stock having an aggregate offering price of up to \$ 15.0 million, subject to the terms and conditions of the December 2021 ATM Agreement. The offering will terminate upon the earlier of (i) December 10, 2024 and (ii) termination of the December 2021 ATM Agreement as permitted therein.

On February 2, 2022, the Company entered into an amendment to the December 2021 ATM Agreement, pursuant to which, the aggregate offering amount of the shares of the Company's common stock which the Company may sell and issue through Ladenburg, as the sales agent, was increased from \$ 15.0 million to \$ 75.0 million (the "ATM Upsize").

As of December 31, 2023, the Company has issued 55,222,809 shares under the ATM Agreement for a total net proceeds of \$ 56.1 million.

***Noncontrolling Interest***

As a result of the merger on November 3, 2021 between Napo EU and Dragon SPAC, the Company assumed a noncontrolling interest amounting to \$ 242,000 as of December 31, 2021 which represents noncontrolling interest held by an investor in Napo Therapeutics.

For the year ended December 31, 2023, noncontrolling interest increased by \$ 635,000 due to additional investment, net of share in comprehensive losses. For the year ended December 31, 2022, noncontrolling interest decreased by \$ 941,000 due to the share in net loss.

**11. Stock-Based Compensation**

***2013 Equity Incentive Plan***

In November 2013, the Company's board of directors and sole stockholder adopted the Jaguar Health, Inc. 2013 Equity Incentive Plan (the "2013 Plan"). The 2013 Plan allows the Company's board of directors to grant stock options, restricted stock awards and restricted stock unit awards to employees, officers, directors and consultants of the Company. Following the effective date of the IPO and after effectiveness of any grants under the 2013 Plan that were contingent on the IPO, no additional stock awards will be granted under the 2013 Plan. Outstanding grants continue to be exercisable, however, any unissued shares under the plan and any forfeitures of outstanding options do not rollover to the 2014 Stock Incentive Plan. There were zero and two option shares outstanding at December 31, 2023 and 2022, respectively.

**2014 Stock Incentive Plan**

Effective May 12, 2015, the Company adopted the Jaguar Health, Inc. 2014 Stock Incentive Plan ("2014 Plan"). The 2014 Plan provides for the grant of options, restricted stock and restricted stock units to eligible employees, directors and consultants to purchase the Company's common stock. The term of an incentive stock option may not exceed 10 years , except that with respect to any participant who owns more than 10% of the voting power of all classes or our outstanding stock, the term must not exceed 5 years . The 2014 Plan provides for automatic share increases on the first day of each fiscal year in the amount of 2 % of the outstanding number of shares of the Company's common stock on last day of the preceding calendar year. The 2014 Plan replaced the 2013 Plan except that all outstanding options under the 2013 Plan remain outstanding until exercised, cancelled or expired.

On April 13, 2022, the Board of Directors of the Company approved a Registration Statement to register an additional 2,417,660 shares of the Company's common stock for issuance pursuant to the awards granted under the 2014 Plan.

As of December 31, 2023, there were 26,262 options outstanding and 127,854 options available for grant. As of December 31, 2022, there were 26,553 options outstanding and 116,011 options available for grant.

**2020 New Employee Inducement Award Plan**

Effective June 16, 2020, the Company adopted the Jaguar Health, Inc. New Employee Inducement Award Plan ("2020 Inducement Award Plan") and, subject to the adjustment provisions of the Inducement Award Plan, reserved 2,222 shares of the Company's common stock for issuance pursuant to equity awards granted under the Inducement Award Plan. The term of an incentive stock option may not exceed 10 years , except that with respect to any participant who owns more than 10% of the voting power of all classes or our outstanding stock, the term must not exceed 5 years . The 2020 Inducement Award Plan provides for the grant of non-statutory stock options, restricted stock units, restricted stock, and performance shares. The 2020 Inducement Award Plan was adopted without stockholder approval pursuant to Rule 5635(c)(4) of the Nasdaq Listing Rules. The terms and conditions of the 2020 Inducement Award Plan are substantially similar to the Company's 2014 Stock Incentive Plan, but with such other terms and conditions intended to comply with the Nasdaq inducement award rules. In accordance with Rule 5635(c)(4) of the Nasdaq Listing Rules, the only persons eligible to receive grants of equity awards under the Inducement Award Plan are individuals who were not previously an employee or director of the Company, or following a bona fide period of non-employment, as an inducement material to such persons entering into employment with the Company.

On April 13, 2022, the Board of Directors of the Company approved an amendment to the 2020 Inducement Award Plan to reserve an additional 471,833 shares of the Company's common stock for issuance pursuant to equity awards granted under the Inducement Award Plan, thereby increasing the number of shares of the Company's common stock issuable thereunder from 500,000 shares to 971,833 shares.

As of December 31, 2023, there were 1,512 options outstanding and 498,488 options available for grant. As of December 31, 2022, there were 1,546 options outstanding and 6,967 options available for grant. The Company authorized an additional 491,481 shares for the stock incentive plans.

**Stock Options and Restricted Stock Units ("RSUs")**

The following table summarized the incentive plan activity for the year ended December 31, 2023 and 2022:

(in thousands, except share and per share data)	Shares Available for Grant	Stock Options Outstanding	RSUs Outstanding	Weighted Average Stock Option Exercise Price	Weighted Average Remaining Contractual Life (Years)	Aggregate Intrinsic Value*
Outstanding at January 1, 2022	8,417	33,286	6,499	\$ 707.97	8.35	\$ 3
Additional shares authorized	151,079	—	—	—	—	—
Options granted	( 44 )	44	—	23.46	—	—
Options exercised	—	—	—	—	—	—
Options canceled	5,251	( 5,251 )	—	418.34	—	—
RSUs granted	( 41,725 )	—	41,725	—	—	—
RSUs vested and released	—	—	( 2,516 )	—	—	—
RSUs cancelled	—	—	( 843 )	—	—	—
Outstanding at December 31, 2022	<u>122,978</u>	<u>28,079</u>	<u>44,865</u>	<u>\$ 592.73</u>	<u>7.19</u>	<u>\$ —</u>
Additional shares authorized	3,166,330	—	—	—	—	—
Options granted	—	—	—	—	—	—
Options exercised	—	—	—	—	—	—
Options canceled	305	( 305 )	—	327.81	—	—
RSUs granted	( 2,690,320 )	—	2,690,320	—	—	—
RSUs excercised	21,808	—	( 21,808 )	—	—	—
RSUs cancelled	5,241	—	( 5,241 )	—	—	—
Outstanding at December 31, 2023	<u>626,342</u>	<u>27,774</u>	<u>2,708,136</u>	<u>\$ 596</u>	<u>6.21</u>	<u>\$ —</u>
Exercisable at December 31, 2023		<u>27,369</u>		<u>\$ 599.12</u>	<u>6.19</u>	<u>\$ —</u>
Vested and expected to vest at December 31, 2023		<u>27,761</u>		<u>\$ 595.76</u>	<u>6.21</u>	<u>\$ —</u>

\*Fair market value of Jaguar stock on December 31, 2023 was \$ 0.15 per share.

The intrinsic value is calculated as the difference between the exercise price of the underlying options and the fair market value of the Company's common stock for options that were in-the-money.

The number of options exercised during the year ended December 31, 2023 and 2022 were zero, respectively.

The weighted average grant date fair value of stock options granted was zero and \$ 22.04 per share during the years ended December 31, 2023, and 2022, respectively.

The number of options that vested in the years ended December 31, 2023, and 2022 was 1,524 and 7,492, respectively. The grant date weighted average fair value of options that vested in the years ended December 31, 2023, and 2022 was \$ 273.62 and \$ 304.57, respectively.

**Stock-Based Compensation**

The following table summarizes stock-based compensation expense related to stock options, inducement stock options and RSUs for the years ended December 31, 2023 and 2022, and are included in the consolidated statements of operations as follows:

(in thousands)	Year Ended December 31,	
	2023	2022
Research and development expense	\$ 1,044	\$ 1,263
Sales and marketing expense	152	267
General and administrative expense	916	1,788
<b>Total</b>	<b>\$ 2,112</b>	<b>\$ 3,318</b>

As of December 31, 2023, the Company had \$ 116,736 of unrecognized stock-based compensation expense for options and RSU's, which is expected to be recognized over a weighted-average period of 0.35 years.

The fair value of options granted during the years ended December 31, 2023 and 2022, respectively, were calculated using the range of assumptions set forth below:

	December 31, 2023	December 31, 2022
Volatility	—	164.0 %
Expected term (years)	—	5.0
Risk-free interest rate	—	3.2 %
Expected dividend yield	—	—

**401(k) Plan**

The Company sponsors a 401(k) defined contribution plan covering all employees. There were no employer contributions to the plan from plan inception through December 31, 2023.

**12. Net Loss Per Share Attributable to Common Stockholders**

The following table presents the calculation of basic and diluted net loss per common share for the years ended December 31, 2023 and 2022:

(in thousands, except share and per share data)	Year Ended December 31,	
	2023	2022
Net loss attributable to common stockholders	\$ (41,300)	\$ (47,454)
Shares used to compute net loss per common share, basic and diluted	23,068,423	1,311,519
Net loss per share attributable to common shareholders, basic and diluted	\$ (1.79)	\$ (36.18)

Basic net loss per share is calculated by dividing net loss by the weighted-average number of common shares outstanding during the period. Diluted net loss per share is computed by dividing net loss by the weighted-average number of shares of common stock, convertible preferred stock, and certain common share equivalents outstanding for the period. Common stock equivalents are only included when their effect is dilutive. The Company's potential securities which include Standstill warrants, PIPE warrants, Royal Global Amendment Exchange warrants and convertible preferred series stock and other common stock equivalents were excluded because their effect is anti-

dilutive. For the prior periods presented, there is no difference in the number of shares used to compute basic and diluted shares outstanding.

The following are the other common stock equivalents of the Company for years ended December 31, 2023 and December 31, 2022:

	December 31, 2023	December 31, 2022
Options issued and outstanding	26,262	26,533
Inducement options issued and outstanding	1,512	1,546
Restricted stock units issued and outstanding	2,708,136	44,865
Warrants issued and outstanding	11,424,807	7,505
<b>Total</b>	<b>14,160,717</b>	<b>80,449</b>

As of April 1, 2024, there were 202,803,012 shares of common stock issued after the balance sheet date.

### 13. Income Taxes

The Company's loss before provision for income taxes during the years ended December 31, 2023 and 2022, was a domestic loss of \$ 35.6 million and \$ 42.1 million, and a foreign loss of \$ 6.3 million and \$ 6.3 million, respectively.

The effective tax rate for 2023 and 2022 was 0 %. As a result of the Company's history of net operating losses ("NOL") and a full valuation allowance against its deferred tax assets, there was minimal current income tax and no deferred income tax provision for the years ended December 31, 2023 and 2022.

The Company's effective tax during the years ended December 31, 2023 and 2022, differed from the federal statutory rate as follows:

	December 31, 2023	2022
Statutory rate	( 21.0 )%	( 21.0 )%
State taxes	( 2.0 )%	( 1.8 )%
Intercompany transactions	1.0 %	0.2 %
Valuation allowance	20.7 %	18.3 %
Nondeductible warrant expense	— %	( 0.3 )%
Book loss on debt extinguishment	( 1.9 )%	1.0 %
Foreign rate differential	( 1.8 )%	( 0.7 )%
Other	4.9 %	4.3 %
<b>Effective tax rate</b>	<b>— %</b>	<b>— %</b>

Net deferred tax assets as of December 31, 2023 and 2022 consisted of the following:

(In thousands)	December 31,	
	2023	2022
<b>Non-current deferred tax assets:</b>		
Net operating losses	\$ 51,853	\$ 24,773
Tax credits	241	241
Stock compensation	559	3,042
Other	4,981	1,006
	57,634	29,062
<b>Valuation allowance</b>	<b>( 56,222 )</b>	<b>( 28,454 )</b>
<b>Net non-current deferred tax assets</b>	<b>1,412</b>	<b>608</b>
<b>Non-current deferred tax liabilities:</b>		
Other	( 1,431 )	( 566 )
Property and equipment	19	( 42 )
Net non-current deferred tax liability	( 1,412 )	( 608 )
<b>Net non-current deferred tax asset (liability)</b>	<b>\$ —</b>	<b>\$ —</b>

A valuation allowance is provided when it is more likely than not that the deferred tax assets will not be realized. The Company has established a valuation allowance to offset net deferred tax assets as of December 31, 2023 and 2022, due to the uncertainty of realizing future tax benefits from its NOL carryforwards and other deferred tax assets.

The valuation allowance increased by \$ 27.4 million during the year ended December 31, 2023.

As of December 31, 2023, the Company had federal and California NOL carryovers of approximately \$

209.9

million and \$ 29.4 million, respectively. Of the federal NOL, \$ 20.7 million will begin to expire in 2034 and \$ 122.5 million will carryforward indefinitely. The California NOL will begin to expire in 2033.

As of December 31, 2023, the Company had California research credit carryovers of approximately \$ 382,000 . The California research credits carry forward indefinitely. The Company had no Federal research credit carryovers.

Utilization of the domestic NOL and tax credit forwards may be subject to a substantial annual limitation due to ownership change limitations that may have occurred or that could occur in the future, as required by the Internal Revenue Code Section 382, as well as similar state provisions. In general, an "ownership change," as defined by the code, results from a transaction or series of transactions over a three-year period resulting in an ownership change of more than 50 percentage points of the outstanding stock of a company by certain stockholders or public groups. Any limitation may result in expiration of all or a portion of the NOL or tax credit carryforwards before utilization. The Company has previously reduced its federal and California R&D credit carryforwards by \$ 1.4 million and \$ 697,000 , respectively.

Enacted on March 27, 2020, the Coronavirus Aid, Relief, and Economic Security Act ("the CARES Act") authorizes more than \$2.0 trillion to battle COVID-19 and its economic effects, including immediate cash relief for individual citizens, loan programs for small business, support for hospitals and other medical providers, and various types of economic relief for impacted businesses and industries. The CARES Act does not have a material impact on the Company's financial results for the year ended December 31, 2023 and 2022.

The Consolidated Appropriations Act, 2021 (the "Act") was enacted in the US on December 27, 2020. The Act enhances and expands certain provisions of the CARES Act. The Act does not have a material impact on the Company's financial results for the year ended December 31, 2023 and 2022.

**Uncertain Tax Positions**

The Company has adopted the provisions of ASC 740, *Income Taxes Related to Uncertain Tax Positions*. Under these principals, tax positions are evaluated in a two-step process. The Company first determines whether it is more-likely-than-not that a tax position will be sustained upon examination. If a tax position meets the more-likely-than-not recognition threshold it is then measured to determine the amount of benefit to be recognized in the financial statements. The tax position is measured as the largest amount of benefit that has a greater than 50 percent likelihood of being realized upon ultimate settlement.

As of December 31, 2023, all unrecognized tax benefits were offset against deferred tax assets which are subject to a full valuation allowance, and if recognized, will not affect the Company's tax rate.

The Company does not anticipate that the total amounts of unrecognized tax benefits will significantly increase or decrease in the next 12 months.

The Company's policy is to include interest and penalties related to unrecognized tax benefits within its provision for income taxes. Due to the Company's net operating loss position, the Company has not recorded an accrual for interest or penalties related to uncertain tax positions for the years ended December 31, 2023 or 2022.

The following is a reconciliation of the beginning and ending amount of the Company's total gross unrecognized tax benefit liabilities:

(in thousands)	December 31,	
	2023	2022
Gross Unrecognized Tax Benefit--Beginning Balance	\$ 77	\$ 77
Increases Related to Tax Positions from Prior Years	—	—
Increases Related to Tax Positions Taken During the Current Year	—	—
Gross Unrecognized Tax Benefit--Ending Balance	<u>\$ 77</u>	<u>\$ 77</u>

**14. Segment Data**

The Company has two reportable segments-human health and animal health. The animal health segment is focused on developing and commercializing prescription and non-prescription products for companion and production animals. The human health segment is focused on developing and commercializing of human products and the ongoing commercialization of Mytesi, which is approved by the FDA for the symptomatic relief of non-infectious diarrhea in adults with HIV/AIDS on antiretroviral therapy.

The Company's reportable segments net revenues and net loss for the years ended December 31, 2023 and 2022 consisted of the following:

(in thousands)	Year Ended December 31,	
	2023	2022
<b>Revenue from external customers</b>		
Human Health	\$ 9,588	\$ 11,741
Animal Health	173	215
Consolidated Totals	<u>\$ 9,761</u>	<u>\$ 11,956</u>
<b>Segment net loss</b>		
Human Health	\$ (21,655)	\$ (18,278)
Animal Health	(20,246)	(30,117)
Consolidated Totals	<u>\$ (41,901)</u>	<u>\$ (48,395)</u>

The Company's reportable segments assets consisted of the following:

	December 31, 2023	December 31, 2022
(in thousands)		
<b>Segment assets</b>		
Human Health	\$ 42,289	\$ 40,898
Animal Health	<u>153,190</u>	<u>128,607</u>
Total	<u><u>\$ 195,479</u></u>	<u><u>\$ 169,505</u></u>

The reconciliation of segments assets to the consolidated assets is as follows:

	December 31, 2023	December 31, 2022
(in thousands)		
Total assets for reportable segments	\$ 195,479	\$ 169,505
Less: Investment in subsidiary	( 29,232 )	( 29,232 )
Less: Intercompany loan	( 115,484 )	( 92,821 )
Consolidated Totals	<u><u>\$ 50,763</u></u>	<u><u>\$ 47,452</u></u>

## **15. Subsequent Events**

### ***December 2021 ATM Agreement***

From January 1, 2024 to April 1, 2024 the Company issued an aggregate of 133,631,424 shares of common stock under the December 2021 ATM Agreement for total net proceeds of \$ 11.6 million.

### ***Series I Convertible Preferred Stock***

On January 15, 2024, Uptown converted 56 shares of Series I Preferred Stock into 2,696,456 shares of common stock.

### ***3a9 Exchanges***

On January 29, 2024, the Company entered into an exchange agreement with Iliad pursuant to which the Company issued an aggregate of 8,000,000 shares of the Company's common stock to Iliad in exchange for \$ 900,800 reduction in the outstanding balance of the October 2020 Royalty Interest. Additionally, the Company entered into an exchange agreement with Streeterville, which the Company issued an aggregate of 1,587,632 shares of the Company's common stock in exchange for \$ 179,000 reduction in the outstanding balance of the August 2022 Royalty Interest.

### ***PIPE Warrant Exchanges***

On February 27, 2024, pursuant to the PIPE Purchase Agreement, each of the PIPE investors entered into an exchange agreement with the Company (each, a "PIPE Warrant Exchange Agreement" and collectively, the "PIPE Warrant Exchange Agreements"). Pursuant to the PIPE Warrant Exchange Agreements, the Company agreed to exchange the PIPE Warrants for shares of common stock at an exchange ratio of 1-for-2.5 ("PIPE Warrant Exchange Transaction"). Upon completion of the PIPE Warrant Exchange Transaction, the Company exchanged the PIPE Warrants to purchase up to 7,535,000 shares of Common Stock for 18,837,500 shares of Common Stock (the "PIPE Exchange Shares"), and the PIPE Warrants were terminated. The PIPE Exchange Shares would be subject to a twelve-month lock-up, and any other equity security of the Company other than the PIPE Exchange Shares owned by the PIPE investors as of the date of the PIPE Warrant Exchange Agreement would be subject to a six-month lock-up.

On February 29, 2024, the PIPE investors converted 122 shares of Series G preferred stock into 3,050,000 shares of common stock subject to a six-month lock-up.

### ***March 2021 Purchase Agreement Extinguishment and Streeterville Exchange***

On March 1, 2024, the Company entered into a privately negotiated exchange agreement with Streeterville (the "Streeterville Exchange Agreement"), pursuant to which the Company issued an aggregate of 179.3822 shares of Series J Preferred Stock to Streeterville at an effective exchange price per share equal to the market price (defined as the Minimum Price under Nasdaq Listing Rule 5635(d)) as of the date of the Streeterville Exchange Agreement, in exchange for the surrender of the March 2021 Purchase Agreement by Streeterville (the "Streeterville Exchange Transaction"). Upon completion of the Streeterville Exchange Transaction, all outstanding balance of the March 2021 Purchase Agreement was fully paid and the March 2021 Purchase Agreement was terminated.

### ***Series J Convertible Preferred Stock***

On March 5, 2024, the Company issued 10,000,000 shares of the Company's common stock to Streeterville in exchange for the surrender and cancellation of 40 shares of Series J Perpetual Preferred Stock. Subsequently, on March 19, 2024, the Company issued 8,333,333 shares of the Company's common stock in exchange for the surrender and cancellation of another 40 shares of Series J Perpetual Preferred Stock.

**Securities Purchase Agreement**

On March 18, 2024, the Company entered into a privately negotiated securities purchase agreement (the "Securities Purchase Agreement") with Gen Ilac Ve Saglik Urunleri Sanayi Ve Ticaret, A.S. (the "Purchaser"), pursuant to which the Company issued 16,666,666 shares of the Company's common stock at a price of \$ 0.12 per share for gross proceeds of approximately \$ 2.0 million. The sale of the securities was consummated in connection with the Licensing Agreement (as defined below).

**Licensing Agreement**

On March 20, 2024, the Company had signed a binding term sheet covering the exclusive license and commercialization agreement for the Company's FDA-approved prescription drug crofelemer with Gen Ilac Ve Saglik Urunleri Sanayi Ve Ticaret, A.S. (the "Purchaser") in certain countries within Eastern Europe (the "Licensing Agreement"). Aside from the Securities Purchase Agreement, The Licensing Agreement entails payment of royalties to Jaguar on all finished crofelemer products sold in the licensed territory, and transfer pricing terms for crofelemer supplied by Jaguar.

**ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE**

None.

**ITEM 9A. CONTROLS AND PROCEDURES**

**Disclosure Controls and Procedures**

Our management, Chief Executive Officer and Principal Financial and Accounting Officer, evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2023. The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by us in the reports that we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms.

Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by us in the reports that we file or submit under the Exchange Act is accumulated and communicated to our management, including our Chief Executive Officer and Principal Financial and Accounting Officer, as appropriate, to allow timely decisions regarding required disclosure. Based on this evaluation, our Chief Executive Officer and Principal Financial and Accounting Officer concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of December 31, 2023.

**Internal Control Over Financial Reporting**

Our management is responsible for establishing and maintaining adequate internal control over financial reporting as defined in Rule 13a-15(f) and 15d-15(c) under the Exchange Act. Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Projections of any evaluation of the effectiveness of internal control to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with policies or procedures may deteriorate. Under the supervision and with the participation of our management, including our Chief Executive Officer and Principal Financial and Accounting Officer, we conducted an evaluation of the effectiveness of our internal control over financial reporting as of December 31, 2023 using the criteria established in Internal Control-Integrated Framework ("2013 Framework") issued by the Committee of Sponsoring Organization of the Treadway Commission ("COSO"). Based on our evaluation using those criteria, our management has concluded that, as of December 31, 2023, our internal control over financial reporting was effective to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles for the reasons discussed above.

This Annual Report on Form 10-K does not include an attestation report of our registered public accounting firm on our internal control over financial reporting because we are an SRC and are not subject to auditor attestation requirements under applicable SEC rules.

**Changes in Internal Control over Financial Reporting**

Other than the changes disclosed above regarding the remediation efforts to address the material weaknesses, there were no changes in our internal control over financial reporting that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting during the year ended December 31, 2023.

**ITEM 9B. OTHER INFORMATION**

None.

**PART III**

**ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE**

The information required by this item is incorporated by reference from the Proxy Statement for the 2024 Annual Meeting of Stockholders to be filed with the SEC within 120 days of the fiscal year ended December 31, 2023.

**ITEM 11. EXECUTIVE COMPENSATION**

The information required by this item is incorporated by reference from the information under the captions "Compensation of Directors and Executive Officers" contained in the Proxy Statement for the 2024 Annual Meeting of Stockholders to be filed with the SEC within 120 days of the fiscal year ended December 31, 2023.

**ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS**

The information required by this item is incorporated by reference from the information under the captions "Security Ownership of Certain Beneficial Owners and Management" and "Compensation of Directors and Executive Officers—Equity Compensation" contained in the Proxy Statement for the 2024 Annual Meeting of Stockholders to be filed with the SEC within 120 days of the fiscal year ended December 31, 2023.

**ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE**

The information required by this item is incorporated by reference from the information under the caption "Proposal 1—Election of Directors—Director Independence" and "Certain Relationships and Related Transactions" contained in the Proxy Statement for the 2022 Annual Meeting of Stockholders to be filed with the SEC within 120 days of the fiscal year ended December 31, 2023.

**ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES**

The information required by this item is incorporated by reference from the information under the caption "Proposal 2—Ratification of the Appointment of Independent Registered Public Accounting Firm—Principal Accountant Fees and Services" contained in the Proxy Statement for the 2024 Annual Meeting of Stockholders to be filed with the SEC within 120 days of the fiscal year ended December 31, 2023.

**PART IV****ITEM 15. EXHIBITS, FINANCIAL STATEMENT SCHEDULES**

Exhibit No.	Description
2.1	<a href="#">Agreement and Plan of Merger, dated as of March 31, 2017, by and among Jaguar Health, Inc. (f/k/a Jaguar Animal Health, Inc.), Napo Acquisition Corporation, Napo Pharmaceuticals, Inc. and Gregory Stock (incorporated by reference to Exhibit 2.1 to the Current Report on Form 8-K of Jaguar Health, Inc. filed March 31, 2017, File No. 001-36714).</a>
3.1	<a href="#">Third Amended and Restated Certificate of Incorporation (incorporated by reference to Exhibit 3.1 to the Current Report on Form 8-K (No. 001-36714) filed with the Securities and Exchange Commission on August 1, 2017).</a>
3.2	<a href="#">Certificate of Amendment of the Third Amended and Restated Certificate of Incorporation (incorporated by reference to Exhibit 3.2 to the Annual Report on Form 10-K filed with the Securities and Exchange Commission on April 9, 2018).</a>
3.3	<a href="#">Certificate of Second Amendment of the Third Amended and Restated Certificate of Incorporation (incorporated by reference to Exhibit 3.1 to the Current Report on Form 8-K filed with the Securities and Exchange Commission on June 1, 2018).</a>
3.4	<a href="#">Certificate of Third Amendment of the Third Amended and Restated Certificate of Incorporation (incorporated by reference to Exhibit 3.2 to the Current Report on Form 8-K filed with the Securities and Exchange Commission on June 1, 2018).</a>
3.5	<a href="#">Certificate of Fifth Amendment of the Third Amended and Restated Certificate of Incorporation (incorporated by reference to Exhibit 3.1 to the Current Report on Form 8-K filed with the Securities and Exchange Commission on June 6, 2019).</a>
3.6	<a href="#">Amended and Restated Bylaws (incorporated by reference to Exhibit 3.2 to the Current Report on Form 8-K (No. 001-36714) filed with the Securities and Exchange Commission on May 18, 2015).</a>
3.7	<a href="#">Certificate of Designation of Series C Perpetual Preferred Stock (incorporated by reference to Exhibit 3.1 to the Current Report on Form 8-K (No. 001-036714) filed with the Securities and Exchange Commission on September 2, 2020).</a>
3.8	<a href="#">Certificate of Designation of Series D Perpetual Preferred Stock (incorporated by reference to Exhibit 3.2 to the Current Report on Form 8-K (No. 001-036714) filed with the Securities and Exchange Commission on September 2, 2020).</a>
3.9	<a href="#">Certificate of Retirement of Series A Convertible Participating Preferred Stock, Series B Convertible Preferred Stock and Series B-1 Convertible Preferred Stock of Jaguar Health, Inc. (incorporated by reference to Exhibit 3.1 to the Current Report on Form 8-K (No. 001-036714) filed with the Securities and Exchange Commission on September 9, 2020).</a>
3.10	<a href="#">Corrected Certificate of Amendment of the Third Amended and Restated Certificate of Incorporation (incorporated by reference to Exhibit 3.1 to the Form 8-K of Jaguar Health, Inc. filed December 10, 2020, File No. 001-36714).</a>
3.11	<a href="#">Certificate of Fifth Amendment of the Third Amended and Restated Certificate of Incorporation of Jaguar Health, Inc. (incorporated by reference to Exhibit 3.1 to the Form 8-K of Jaguar Health, Inc. filed September 3, 2021, File No. 001-36714).</a>
3.12	<a href="#">First Amendment to the Amended and Restated Bylaws, dated March 17, 2022. (incorporated by reference to Exhibit 3.1 to the Form 8-K of Jaguar Health, Inc. filed March 18, 2022, File No. 001-36714).</a>
3.13	<a href="#">Certificate of Designation of Series E Preferred Stock. (incorporated by reference to Exhibit 3.1 to the Form 8-K of Jaguar Health, Inc. filed August 23, 2022, File No. 001-36714).</a>
3.14	<a href="#">Certificate of Sixth Amendment of the Third Amended and Restated Certificate of Incorporation of Jaguar Health, Inc. (incorporated by reference to Exhibit 3.1 to the Form 8-K of Jaguar Health, Inc. filed September 30, 2022, File No. 001-36714).</a>
3.15	<a href="#">Certificate of Designation of Series F Preferred Stock. (incorporated by reference to Exhibit 3.1 to the Form 8-K of Jaguar Health, Inc. filed November 16, 2022, File No. 001-36714).</a>

Exhibit No.	Description
3.16	<a href="#">Certificate of Seventh Amendment of the Third Amended and Restated Certificate of Incorporation of Jaguar Health, Inc. (incorporated by reference to Exhibit 3.1 to the Form 8-K of Jaguar Health, Inc. filed January 23, 2023, File No. 001-36714).</a>
3.17	<a href="#">Certificate of Designation of Series G Convertible Preferred Stock. (incorporated by reference to Exhibit 3.1 to the Form 8-K of Jaguar Health, Inc. filed May 9, 2023, File No. 001-36714).</a>
3.18	<a href="#">Certificate of Designation of Series H Convertible Preferred Stock. (incorporated by reference to Exhibit 3.1 to the Form 8-K of Jaguar Health, Inc. filed July 3, 2023, File No. 001-36714).</a>
3.19	<a href="#">Certificate of Designation of Series I Convertible Preferred Stock. (incorporated by reference to Exhibit 3.1 to the Form 8-K of Jaguar Health, Inc. filed October 5, 2023, File No. 001-36714).</a>
3.20	<a href="#">Certificate of Designation of Series J Convertible Preferred Stock. (incorporated by reference to Exhibit 3.1 to the Form 8-K of Jaguar Health, Inc. filed March 1, 2024, File No. 001-36714).</a>
4.1	<a href="#">Specimen Non-Voting Common Stock Certificate of Jaguar Health, Inc. (incorporated by reference to Exhibit 4.1 to the Form 8-K of Jaguar Health, Inc. filed August 1, 2017, File No. 001-36714).</a>
4.2	<a href="#">Common Stock Warrant, dated August 28, 2018, by and between Jaguar Health, Inc. and the holder named therein (incorporated by reference to Ex. 4.1 to the Current Report on Form 8-K filed on September 4, 2018).</a>
4.3	<a href="#">Common Stock Warrant, dated September 11, 2018, by and between Jaguar Health, Inc. and L2 Capital, LLC (incorporated by reference to Ex. 4.3 to the Current Report on Form 8-K filed on September 12, 2018).</a>
4.4	<a href="#">Common Stock Warrant, dated September 11, 2018, by and between Jaguar Health, Inc. and Charles Conte (incorporated by reference to Ex. 4.4 to the Current Report on Form 8-K filed on September 12, 2018).</a>
4.5	<a href="#">Form of Pre-Funded Warrant (incorporated by reference to Exhibit 4.6 to the Registration Statement on Form S-1 (No. 333-227292) filed with the Securities and Exchange Commission on October 1, 2018).</a>
4.6	<a href="#">Form of Common Stock Warrant (incorporated by reference to Exhibit 4.3 to the Form 8-K of Jaguar Health, Inc. filed March 22, 2019).</a>
4.7	<a href="#">Form of Placement Agent Warrant (incorporated by reference to Exhibit 4.1 to the Form 8-K/A of Jaguar Health, Inc. filed March 26, 2019).</a>
4.8	<a href="#">Form of LOC Common Stock Warrant (incorporated by reference to Exhibit 4.1 to the Form 8-K of Jaguar Health, Inc. filed April 4, 2019, File No. 001-36714).</a>
4.9	<a href="#">Specimen Common Stock Certificate of Jaguar Health, Inc. (incorporated by reference to Exhibit 4.1 to the Form 8-K of Jaguar Health, Inc. filed June 1, 2018, File No. 001-36714).</a>
4.10	<a href="#">Form of Series 1 Warrant (incorporated by reference to Exhibit 4.1 to the Form 8-K of Jaguar Health, Inc. filed July 23, 2019, File No. 001-36714).</a>
4.11	<a href="#">Form of Series 2 Warrant (incorporated by reference to Exhibit 4.2 to the Form 8-K of Jaguar Health, Inc. filed July 23, 2019, File No. 001-36714).</a>
4.12	<a href="#">Promissory Note, dated October 1, 2019, between Napo Pharmaceuticals, Inc. and Michael Tempesta (incorporated by reference to Exhibit 4.1 to the Form 8-K of Jaguar Health, Inc. filed October 7, 2019, File No. 001-36714).</a>
4.13	<a href="#">Form of Pre-Funded Common Stock Purchase Warrant (incorporated by reference to Exhibit 4.1 to the Form 8-K of Jaguar Health, Inc. filed November 14, 2019, File No. 001-36714).</a>
4.14	<a href="#">Form of Common Stock Purchase Warrant (incorporated by reference to Exhibit 4.1 to the Form 8-K of Jaguar Health, Inc. filed December 26, 2019, File No. 001-36714).</a>
4.15	<a href="#">Royalty Interest, dated March 4, 2020, by and between the Company and Iliad Research and Trading L.P. (incorporated by reference to Exhibit 4.1 to the Form 8-K of Jaguar Health, Inc. filed March 6, 2020, File No. 001-36714).</a>
4.16	<a href="#">Description of the Registrant's Securities Registered Pursuant to Section 12 of the Securities Exchange Act of 1945, as amended (incorporated herein by reference to Exhibit 4.26 to the Annual Report on Form 10-K filed on April 3, 2020).</a>
4.17	<a href="#">Form of Series 3 Common Stock Purchase Warrant (incorporated by reference to Exhibit 4.1 to the Form 8-K of Jaguar Health, Inc. filed May 22, 2020).</a>

Exhibit No.	Description
4.18	<a href="#">Global Amendment, dated September 1, 2020, by and among Jaguar Health, Inc., Napo Pharmaceuticals, Inc. and Chicago Ventures, L.P. (incorporated by reference to Exhibit 4.1 to the Form 8-K of Jaguar Health, Inc. filed September 2, 2020).</a>
4.19	<a href="#">Royalty Interest, dated October 8, 2020, by and between Jaguar Health, Inc. and Iliad Research and Trading, L.P. (incorporated by reference to Exhibit 4.1 to the Form 8-K of Jaguar Health, Inc. filed October 9, 2020).</a>
4.20	<a href="#">Form of Pre-Funded Common Stock Purchase Warrant (incorporated by reference to Exhibit 4.1 to the Form 8-K of Jaguar Health, Inc. filed October 9, 2020).</a>
4.21	<a href="#">Royalty Interest, dated December 22, 2020, by and between Jaguar Health, Inc. and Irving Park Capital, LLC (incorporated by reference to Exhibit 4.1 to the Form 8-K filed December 29, 2020, File No. 001-36714).</a>
4.22	<a href="#">Secured Promissory Note, dated January 19, 2021, by and among Jaguar Health, Inc., Napo Pharmaceuticals, Inc. and Streeterville Capital, LLC (incorporated by reference to Exhibit 4.1 to the Form 8-K filed January 22, 2021, File No. 001-36714).</a>
4.23	<a href="#">Common Stock Purchase Warrant, dated April 7, 2021, by and between Jaguar Health, Inc. and Oasis Capital, LLC (incorporated by reference to Exhibit 4.1 to the Form 8-K of Jaguar Health, Inc. filed April 8, 2021, File No. 001-36714).</a>
4.24	<a href="#">Global Amendment, dated April 14, 2022, by and between Jaguar Health, Inc. and Iliad Research and Trading, L.P. (incorporated by reference to Exhibit 4.1 to the Form 8-K of Jaguar Health, Inc. filed April 15, 2022, File No. 001-36714).</a>
4.25	<a href="#">Global Amendment, dated April 14, 2022, by and between Jaguar Health, Inc. and Uptown Capital, LLC (incorporated by reference to Exhibit 4.2 to the Form 8-K of Jaguar Health, Inc. filed April 15, 2022, File No. 001-36714).</a>
4.26	<a href="#">Global Amendment, dated April 14, 2022, by and between Jaguar Health, Inc. and Streeterville Capital, LLC (incorporated by reference to Exhibit 4.3 to the Form 8-K of Jaguar Health, Inc. filed April 15, 2022, File No. 001-36714).</a>
4.27	<a href="#">Global Amendment, dated April 14, 2022, by and among Jaguar Health, Inc., Napo Pharmaceuticals, Inc. and Streeterville Capital, LLC (incorporated by reference to Exhibit 4.4 to the Form 8-K of Jaguar Health, Inc. filed April 15, 2022, File No. 001-36714).</a>
4.28	<a href="#">Royalty Interest, dated August 24, 2022, by and between Jaguar Health, Inc. and Streeterville Capital, LLC. (incorporated by reference to Exhibit 4.1 to the Form 8-K of Jaguar Health, Inc. filed August 30, 2022, File No. 001-36714).</a>
4.29	<a href="#">Form of Common Stock Purchase Warrant (incorporated by reference to Exhibit 4.1 to the Form 8-K of Jaguar Health, Inc. filed May 9, 2023, File No. 001-36714).</a>
4.30	<a href="#">Global Amendment No. 2, dated September 29, 2023, by and between Jaguar Health, Inc. and Iliad Research and Trading, L.P. (incorporated by reference to Exhibit 4.1 to the Form 8-K of Jaguar Health, Inc. filed October 5, 2023, File No. 001-36714).</a>
4.31	<a href="#">Global Amendment No. 2, dated September 29, 2023, by and between Jaguar Health, Inc. and Uptown Capital, LLC (incorporated by reference to Exhibit 4.2 to the Form 8-K of Jaguar Health, Inc. filed October 5, 2023, File No. 001-36714).</a>
4.32	<a href="#">Global Amendment, dated September 29, 2023, by and between Jaguar Health, Inc. and Streeterville Capital, LLC (incorporated by reference to Exhibit 4.3 to the Form 8-K of Jaguar Health, Inc. filed October 5, 2023, File No. 001-36714).</a>
4.33	<a href="#">Global Amendment No. 2, dated September 29, 2023, by and between Jaguar Health, Inc. and Streeterville Capital, LLC (incorporated by reference to Exhibit 4.4 to the Form 8-K of Jaguar Health, Inc. filed October 5, 2023, File No. 001-36714).</a>
4.34	<a href="#">Form of Common Stock Purchase Warrant (incorporated by reference to Exhibit 4.5 to the Form 8-K of Jaguar Health, Inc. filed October 5, 2023, File No. 001-36714).</a>
10.1‡	<a href="#">Form of Indemnification Agreement by and between Jaguar Health, Inc. and its directors and officers (incorporated by reference to Exhibit 10.1 to the Registration Statement on Form S-1 (No. 333-198383) filed with the Securities and Exchange Commission on August 27, 2014).</a>

Exhibit No.	Description
10.2‡	<a href="#">Form of Notice of Grant of Stock Option and Stock Option Agreement under the 2014 Stock Incentive Plan (incorporated by reference to Exhibit 10.6 to the Registration Statement on Form S-1 (No. 333-198383) filed with the Securities and Exchange Commission on August 27, 2014).</a>
10.3‡	<a href="#">Form of Notice of Grant of Restricted Stock and Restricted Stock Agreement under the 2014 Stock Incentive Plan (incorporated by reference to Exhibit 10.7 to the Registration Statement on Form S-1 (No. 333-198383) filed with the Securities and Exchange Commission on August 27, 2014).</a>
10.4‡	<a href="#">Form of Notice of Grant of Restricted Stock Units and Restricted Stock Unit Agreement under the 2014 Stock Incentive Plan (incorporated by reference to Exhibit 10.8 to the Registration Statement on Form S-1 (No. 333-198383) filed with the Securities and Exchange Commission on August 27, 2014).</a>
10.5‡	<a href="#">Offer Letter by and between Jaguar Health, Inc. and Lisa A. Conte, dated March 1, 2014 (incorporated by reference to Exhibit 10.9 to the Registration Statement on Form S-1 (No. 333-198383) filed with the Securities and Exchange Commission on August 27, 2014).</a>
10.6‡	<a href="#">Offer Letter by and between Jaguar Health, Inc. and Steven R. King, Ph.D., dated February 28, 2014 (incorporated by reference to Exhibit 10.11 to the Registration Statement on Form S-1 (No. 333-198383) filed with the Securities and Exchange Commission on August 27, 2014).</a>
10.7†	<a href="#">Formulation Development and Manufacturing Agreement between Jaguar Health, Inc. and Patheon Pharmaceuticals Inc., dated October 8, 2015 (incorporated by reference to Exhibit 10.30 to the Registration Statement on Form S-1 (No. 333-208905) filed with the Securities and Exchange Commission on January 7, 2016).</a>
10.8	<a href="#">Common Stock Warrant issued pursuant to the Letter Agreement, dated November 8, 2016, between Jaguar Health, Inc. and Serious Change II LP, which expires July 28, 2022 (incorporated herein by reference to Exhibit 10.2 to the Quarterly Report on Form 10-Q (No. 001-36714) filed on November 14, 2016).</a>
10.9	<a href="#">Distribution Agreement, dated December 9, 2016, by and between Jaguar Health, Inc. and Henry Schein, Inc. (incorporated herein by reference to Exhibit 10.41 to the Annual Report on Form 10-K filed on February 15, 2017).</a>
10.10	<a href="#">Alliance Agreement, dated May 23, 2005, by and among AsiaPharm Investment Limited and its Affiliates, including Shandong Luye Pharmaceuticals Co. Ltd., and Napo Pharmaceuticals, Inc. (incorporated herein by reference to Exhibit 10.61 to the Registration Statement on Form S-4/A filed May 26, 2017 (No. 333-217364)).</a>
10.11†	<a href="#">Finder's Agreement, dated April 9, 2010, by and among Luye Pharma Group Limited and its Affiliates, including Shandong Luye Pharmaceuticals Co. Ltd., and Napo Pharmaceuticals, Inc. (incorporated herein by reference to Exhibit 10.62 to the Registration Statement on Form S-4/A filed May 26, 2017 (No. 333-217364)).</a>
10.12†	<a href="#">License Agreement, dated February 28, 2007, by and between Insmed Incorporated and Napo Pharmaceuticals, Inc. (incorporated herein by reference to Exhibit 10.77 to the Registration Statement on Form S-4/A filed May 26, 2017 (No. 333-217364)).</a>
10.13†	<a href="#">Amendment, Waiver &amp; Consent, dated June 27, 2017, by and among Jaguar Health, Inc., Nantucket Investments Limited, and Napo Pharmaceuticals, Inc. (incorporated by reference to Ex. 10.83 of the Company's Registration Statement on Form S-4 (Registration No. 333-217364) filed on July 5, 2017).</a>
10.14†	<a href="#">Termination, Asset Transfer and Transition Agreement, dated September 22, 2017, by and between Napo Pharmaceuticals, Inc. and Glenmark Pharmaceuticals, Ltd. (incorporated by reference to Ex. 10.8 to the Quarterly Report on Form 10-Q filed on November 20, 2017).</a>
10.15	<a href="#">Registration Rights Agreement, dated March 23, 2018, by and between Jaguar Health, Inc. and Sagard Capital Partners, L.P. (incorporated by reference to Ex. 10.2 to the Current Report on Form 8-K filed on March 27, 2018).</a>
10.16	<a href="#">Registration Rights Agreement, dated September 11, 2018, by and between Jaguar Health, Inc. and L2 Capital LLC (incorporated by reference to Ex. 10.3 to the Current Report on Form 8-K filed on September 12, 2018).</a>
10.17	<a href="#">Registration Rights Agreement, dated September 11, 2018, by and between Jaguar Health, Inc. and Charles Conte (incorporated by reference to Ex. 10.4 to the Current Report on Form 8-K filed on September 12, 2018).</a>
10.18	<a href="#">Form of Registration Rights Agreement (incorporated by reference to Exhibit 10.2 to the Form 8-K of Jaguar Health, Inc. filed March 22, 2019).</a>

Exhibit No.	Description
10.19	<a href="#">Letter of Credit Cancellation &amp; Warrant Issuance Agreement, dated March 29, 2019, by and between Jaguar Health, Inc. and the letter of credit beneficiary named therein (incorporated by reference to Exhibit 10.1 to the Form 8-K of Jaguar Health, Inc. filed April 4, 2019).</a>
10.20	<a href="#">Amendment No. 1 to Registration Rights Agreement, dated May 30, 2019, by and between Jaguar Health, Inc. and Sagard Capital Partners, L.P. (incorporated by reference to Exhibit 10.120 to the Registration Statement on Form S-1 (No. 333-233989) filed with the Securities and Exchange Commission on September 27, 2019).</a>
10.21	<a href="#">Form of Amendment Agreement (incorporated by reference to Exhibit 10.1 to the Form 8-K of Jaguar Health, Inc. filed July 5, 2019, File No. 001-36714).</a>
10.22#	<a href="#">Master Services Agreement, dated June 24, 2019, by and among Napo Pharmaceuticals, Inc., Integrium, LLC, and POC Capital, LLC (incorporated by reference to Exhibit 10.24 to the Form 10-K of Jaguar Health, Inc. filed on March 31, 2021, File No. 001-36714).</a>
10.23	<a href="#">Form of Exchange Agreement, between Jaguar Health, Inc. and Chicago Venture Partners, L.P. (incorporated by reference to Exhibit 10.6 to the Form 10-Q of Jaguar Health, Inc. filed on August 14, 2019, File No. 001-36714).</a>
10.24	<a href="#">Form of Warrant Agency Agreement between Jaguar Health, Inc. and American Stock Transfer &amp; Trust Company, LLC (incorporated by reference to Exhibit 10.117 to the Form S-1/A of Jaguar Health, Inc. filed on July 15, 2019, File No. 333-231399).</a>
10.25	<a href="#">License Termination and Settlement Termination Agreement, dated October 1, 2019, by and among Jaguar Health, Inc., Napo Pharmaceuticals, Inc. and Michael Tempesta (incorporated by reference to Exhibit 10.1 to the Form 8-K of Jaguar Health, Inc. filed October 7, 2019, File No. 001-36714).</a>
10.26#	<a href="#">Securities Purchase Agreement, dated November 13, 2019, by and between Jaguar Health, Inc. and the purchasers named therein (incorporated by reference to Exhibit 10.1 to the Form 8-K of Jaguar Health, Inc. filed November 14, 2019, File No. 001-36714).</a>
10.27	<a href="#">Securities Purchase Agreement, dated December 20, 2019, by and between Jaguar Health, Inc. and the investors named therein (incorporated by reference to Exhibit 10.1 to the Form 8-K of Jaguar Health, Inc. filed December 26, 2019, File No. 001-36714).</a>
10.28	<a href="#">Form of Warrant Exercise Agreement by and between Jaguar Health, Inc. and the Holder named therein (incorporated by reference to Exhibit 10.1 to the Form 8-K filed February 28, 2020, File No. 001-36714).</a>
10.29	<a href="#">Securities Purchase Agreement, dated March 23, 2020, by and between Jaguar Health, Inc. and the investors named therein (incorporated by reference to Exhibit 10.1 to the Form 8-K filed March 26, 2020, File No. 001-36714).</a>
10.30	<a href="#">Equity Purchase Agreement, dated March 24, 2020, by and between Jaguar Health, Inc. and Oasis Capital, LLC (incorporated by reference to Exhibit 10.4 to the Form 8-K filed March 26, 2020, File No. 001-36714).</a>
10.31	<a href="#">Registration Rights Agreement, dated March 24, 2020, by and between Jaguar Health, Inc. and Oasis Capital, LLC (incorporated by reference to Exhibit 10.5 to the Form 8-K filed March 26, 2020, File No. 001-36714).</a>
10.32‡	<a href="#">Jaguar Health, Inc. 2014 Stock Incentive Plan as amended and restated effective October 1, 2019 (incorporated by reference to Exhibit 10.101 to the Form 10-K of Jaguar Health, Inc. filed April 3, 2020, File No. 001-36714).</a>
10.33	<a href="#">Purchase Agreement, dated April 15, 2020, by and between Napo Pharmaceuticals, Inc. and Atlas Sciences, LLC (incorporated by reference to Exhibit 10.1 to the Form 8-K filed April 16, 2020, File No. 001-36714).</a>
10.34	<a href="#">License Agreement, dated April 15, 2020, by and between Jaguar Health, Inc. and Atlas Sciences, LLC (incorporated by reference to Exhibit 10.2 to the Form 8-K filed April 16, 2020, File No. 001-36714).</a>
10.35	<a href="#">Purchase Agreement, dated May 12, 2020, by and among Jaguar Health, Inc., Napo Pharmaceuticals, Inc. and Oasis Capital, LLC (incorporated by reference to Exhibit 10.1 to the Form 8-K filed May 21, 2020, File No. 001-36714).</a>

Exhibit No.	Description
10.36	<a href="#">Assignment Agreement, dated May 12, 2020, by and between Napo Pharmaceuticals, Inc. and Oasis Capital, LLC (incorporated by reference to Exhibit 10.2 to the Form 8-K filed May 21, 2020, File No. 001-36714).</a>
10.37‡	<a href="#">Jaguar Health, Inc. New Employee Inducement Award Plan (incorporated by reference to Exhibit 10.1 to the Form 8-K filed June 19, 2020, File No. 001-36714).</a>
10.38‡	<a href="#">Form of Notice of Grant of Stock Option and Stock Option Agreement under Jaguar Health, Inc. New Employee Inducement Award Plan (incorporated by reference to Exhibit 10.2 to the Form 8-K filed June 19, 2020, File No. 001-36714).</a>
10.39‡	<a href="#">Form of Notice of Grant of Restricted Stock Units and Restricted Stock Unit Agreement under the Jaguar Health, Inc. New Employee Inducement Award Plan (incorporated by reference to Exhibit 10.3 to the Form 8-K filed June 19, 2020, File No. 001-36714).</a>
10.40	<a href="#">Securities Purchase Agreement, dated March 4, 2020, by and between Jaguar Health, Inc. and Iliad Research and Trading, L.P. (incorporated by reference to Exhibit 10.1 to the Form 8-K filed March 6, 2020, File No. 001-36714).</a>
10.41	<a href="#">First Amendment to Royalty Interest Purchase Agreement and Related Documents, dated July 10, 2020, between Jaguar Health, Inc. and Iliad Research and Trading, L.P. (incorporated by reference to Exhibit 10.1 to the Form 8-K filed July 14, 2020, File No. 001-36714).</a>
10.42‡	<a href="#">Form of Severance and Change of Control Agreement (incorporated by reference to Exhibit 10.11 to the Form 10-Q filed August 13, 2020 File No. 001-36714).</a>
10.43	<a href="#">First Amendment to Purchase Agreement, dated June 26, 2020, by and among Jaguar Health, Inc., Napo Pharmaceuticals, Inc. and Oasis Capital, LLC (incorporated by reference to Exhibit 10.12 to the Form 10-Q filed August 13, 2020 File No. 001-36714).</a>
10.44	<a href="#">First Amendment to Assignment Agreement, dated June 26, 2020, by and between Napo Pharmaceuticals, Inc. and Oasis Capital, LLC (incorporated by reference to Exhibit 10.13 to the Form 10-Q filed August 13, 2020 File No. 001-36714).</a>
10.45	<a href="#">Exchange Agreement, dated September 1, 2020, by and between Jaguar Health, Inc. and Iliad Research and Trading, L.P. (incorporated by reference to Exhibit 10.1 to the Form 8-K filed September 2, 2020, File No. 001-36714).</a>
10.46	<a href="#">Stock Plan Agreement for Payment of Consulting Services, dated September 1, 2020, by and among Jaguar Health, Inc., Sagard Capital Partners Management Corp. and Sagard Capital Partners, L.P. (incorporated by reference to Exhibit 10.2 to the Form 8-K filed September 2, 2020, File No. 001-36714).</a>
10.47	<a href="#">Stock Plan Agreement, dated October 6, 2020, by and between Jaguar Health, Inc. and PoC Capital, LLC (incorporated by reference to Exhibit 10.1 to the Form 8-K filed October 7, 2020, File No. 001-36714).</a>
10.48	<a href="#">Fee Settlement Agreement dated October 7, 2020, by and between Jaguar Health, Inc. and Atlas Sciences, LLC (incorporated by reference to Exhibit 10.1 to the Form 8-K filed October 9, 2020, File No. 001-36714).</a>
10.49	<a href="#">Royalty Interest Purchase Agreement, dated October 8, 2020, by and between Jaguar Health, Inc. and Iliad Research and Trading, L.P. (incorporated by reference to Exhibit 10.1 to the Form 8-K filed October 9, 2020, File No. 001-36714).</a>
10.50	<a href="#">Exchange Agreement, dated October 8, 2020, by and between Jaguar Health, Inc. and Iliad Research and Trading, L.P. (incorporated by reference to Exhibit 10.2 to the Form 8-K filed October 9, 2020, File No. 001-36714).</a>
10.51‡	<a href="#">Office Sublease Agreement, dated August 31, 2020, by and between Jaguar Health, Inc. and Peacock Construction, Inc. (incorporated by reference to Exhibit 10.4 to the Form 10-Q filed November 16, 2020, File No. 001-36714).</a>
10.52	<a href="#">Consent to Sublease Agreement, dated August 31, 2020, by and among M&amp;E, LLC, Jaguar Health, Inc. and Peacock Construction, Inc. (incorporated by reference to Exhibit 10.5 to the Form 10-Q filed November 16, 2020, File No. 001-36714).</a>

Exhibit No.	Description
10.53#	<a href="#">Manufacturing and Supply Agreement, dated September 3, 2020, by and between Glenmark Life Sciences Limited and Napo Pharmaceuticals, Inc. (incorporated by reference to Exhibit 10.6 to the Form 10-Q filed November 16, 2020, File No. 001-36714).</a>
10.54	<a href="#">Securities Purchase Agreement, dated December 22, 2020, by and between Jaguar Health, Inc. and Irving Park Capital, LLC (incorporated by reference to Exhibit 10.1 to the Form 8-K filed December 29, 2020, File No. 001-36714).</a>
10.55	<a href="#">Note Purchase Agreement, dated January 19, 2021, by and among Jaguar Health, Inc., Napo Pharmaceuticals, Inc. and Streeterville Capital, LLC (incorporated by reference to Exhibit 10.1 to the Form 8-K filed January 22, 2021, File No. 001-36714).</a>
10.56	<a href="#">Security Agreement, dated January 19, 2021, by and between Napo Pharmaceuticals, Inc. and Streeterville Capital, LLC (incorporated by reference to Exhibit 10.2 to the Form 8-K filed January 22, 2021, File No. 001-36714).</a>
10.57#	<a href="#">Master Services Agreement, dated October 5, 2020, by and between Napo Pharmaceuticals, Inc. and Integrium, LLC (incorporated by reference to Exhibit 10.67 to the Form 10-K filed March 31, 2021, File No. 001-36714).</a>
10.58	<a href="#">Form of Securities Purchase Agreement (incorporated by reference to Exhibit 10.1 to the Form 8-K of Jaguar Health, Inc. filed January 14, 2021, File No. 001-36714).</a>
10.59#	<a href="#">Office Lease Agreement, dated March 25, 2021, by and between Jaguar Health, Inc. and M &amp; E LLC (incorporated by reference to Exhibit 10.1 to the Form 8-K of Jaguar Health, Inc. filed April 8, 2021, File No. 001-36714).</a>
10.60	<a href="#">First Amendment to the Equity Purchase Agreement, dated April 7, 2021, by and between Jaguar Health, Inc. and Oasis Capital, LLC (incorporated by reference to Exhibit 10.2 to the Form 8-K of Jaguar Health, Inc. filed April 8, 2021, File No. 001-36714).</a>
10.61	<a href="#">Registration Rights Agreement, dated April 7, 2021, by and between Jaguar Health, Inc. and Oasis Capital, LLC (incorporated by reference to Exhibit 10.3 to the Form 8-K of Jaguar Health, Inc. filed April 8, 2021, File No. 001-36714).</a>
10.62	<a href="#">Form of Securities Purchase Agreement, dated April 29, 2021 (incorporated by reference to Exhibit 10.1 to the Form 8-K of Jaguar Health, Inc. filed April 30, 2021, File No. 001-36714).</a>
10.63#	<a href="#">Subscription Agreement, dated June 1, 2021, by and among Dragon SPAC S.p.A., Napo Pharmaceuticals, Inc. and Joshua Mailman (incorporated by reference to Exhibit 10.1 to the Form 8-K of Jaguar Health, Inc. filed June 4, 2021, File No. 001-36714).</a>
10.64#	<a href="#">License Agreement, dated August 18, 2021, by and between Napo Pharmaceuticals, Inc. and Napo EU S.p.A. (incorporated by reference to Exhibit 10.1 to the Form 8-K of Jaguar Health, Inc. filed August 24, 2021, File No. 001-36714).</a>
10.65	<a href="#">Securities Purchase Agreement, dated September 13, 2021, by and between Jaguar Health, Inc. and the investors named therein (incorporated by reference to Exhibit 10.1 to the Form 8-K of Jaguar Health, Inc. filed September 17, 2021, File No. 001-36714).</a>
10.66	<a href="#">At The Market Offering Agreement, dated December 10, 2021, by and between Jaguar Health, Inc. and Ladenburg Thalmann &amp; Co. Inc. (incorporated by reference to Exhibit 10.1 to the Form 8-K of Jaguar Health, Inc. filed December 10, 2021, File No. 001-36714).</a>
10.67	<a href="#">First Amendment to the At The Market Offering Agreement, dated February 2, 2022, by and between Jaguar Health, Inc. and Ladenburg Thalmann &amp; Co. Inc. (incorporated by reference to Exhibit 10.1 to the Form 8-K of Jaguar Health, Inc. filed February 2, 2022, File No. 001-36714).</a>
10.68	<a href="#">First Amendment to the Jaguar Health, Inc. New Employee Inducement Award Plan (incorporated by reference to Exhibit 10.1 to the Form 8-K of Jaguar Health, Inc. filed April 15, 2022, File No. 001-36714).</a>
10.69	<a href="#">First Amendment to the Jaguar Health, Inc. New Employee Inducement Award Plan (incorporated by reference to Exhibit 10.1 to the Form 8-K of Jaguar Health, Inc. filed April 15, 2022, File No. 001-36714).</a>
10.70#	<a href="#">Manufacturing Services Agreement, dated June 10, 2022, by and between Napo Pharmaceuticals, Inc. and Patheon Pharmaceuticals Inc. (incorporated by reference to Exhibit 10.1 to the Form 8-K/A of Jaguar Health, Inc. filed August 24, 2022, File No. 001-36714).</a>

Exhibit No.	Description
10.71	<a href="#">License and Services Agreement, dated June 29, 2022, by and among Jaguar Health, Inc., SynWorld Technologies Corporation, C&amp;E Telecom, LTD and Tao Wang (incorporated by reference to Exhibit 10.1 to the Form 8-K of Jaguar Health, Inc. filed June 29, 2022, File No. 001-36714).</a>
10.72#	<a href="#">Amended and Restated License Agreement, dated July 19, 2022, by and between Napo Pharmaceuticals, Inc. and Napo Therapeutics S.p.A. (incorporated by reference to Exhibit 10.1 to the Form 8-K of Jaguar Health, Inc. filed July 20, 2022, File No. 001-36714).</a>
10.73	<a href="#">Securities Purchase Agreement, dated August 18, 2022, by and between Jaguar Health, Inc. and SynWorld Technologies Corporation (incorporated by reference to Exhibit 10.1 to the Form 8-K of Jaguar Health, Inc. filed August 23, 2022, File No. 001-36714).</a>
10.74	<a href="#">First Amendment to the License and Services Agreement, dated August 18, 2022, by and between Jaguar Health, Inc. and SynWorld Technologies Corporation (incorporated by reference to Exhibit 10.2 to the Form 8-K of Jaguar Health, Inc. filed August 23, 2022, File No. 001-36714).</a>
10.75	<a href="#">Royalty Interest Purchase Agreement, dated August 24, 2022, by and between Jaguar Health, Inc. and Streeterville Capital, LLC (incorporated by reference to Exhibit 10.1 to the Form 8-K of Jaguar Health, Inc. filed August 30, 2022, File No. 001-36714).</a>
10.76	<a href="#">Amended and Restated License and Services Agreement, dated October 11, 2022, by and among Jaguar Health, Inc., SynWorld Technologies Corporation, C&amp;E Telecom, LTD and Tao Wang (incorporated by reference to Exhibit 10.1 to the Form 8-K of Jaguar Health, Inc. October 14, 2022, File No. 001-36714).</a>
10.77	<a href="#">Global Amendment, dated October 17, 2022, by and among Jaguar Health, Inc., Napo Pharmaceuticals, Inc. and Streeterville Capital, LLC (incorporated by reference to Exhibit 10.1 to the Form 8-K of Jaguar Health, Inc. filed October 21, 2022, File No. 001-36714).</a>
10.78	<a href="#">Securities Purchase Agreement, dated November 11, 2022, by and between Jaguar Health, Inc. and SynWorld Technologies Corporation (incorporated by reference to Exhibit 10.1 to the Form 8-K of Jaguar Health, Inc. filed November 16, 2022, File No. 001-36714).</a>
10.79	<a href="#">Form of Company Stock Option Cancellation Agreement (incorporated by reference to Exhibit 10.1 to the Form 8-K of Jaguar Health, Inc. filed December 30, 2022, File No. 001-36714).</a>
10.80	<a href="#">Mutual Termination of License Agreement, dated as of January 31, 2023, by and among Jaguar Health, Inc., SynWorld Technologies Corporation, C&amp;E Telecom, LTD, and Tao Wang (incorporated by reference to Exhibit 10.1 to the Form 8-K of Jaguar Health, Inc. filed February 6, 2023, File No. 001-36714).</a>
10.81	<a href="#">Form of Securities Purchase Agreement, dated May 8, 2023 (incorporated by reference to Exhibit 10.1 to the Form 8-K of Jaguar Health, Inc. filed May 9, 2023, File No. 001-36714).</a>
10.82	<a href="#">Standstill Agreement, dated May 8, 2023 (incorporated by reference to Exhibit 10.2 to the Form 8-K of Jaguar Health, Inc. filed May 9, 2023, File No. 001-36714).</a>
10.83	<a href="#">Second Amendment to the Jaguar Health, Inc. New Employee Inducement Award Plan (incorporated by reference to Exhibit 10.1 to the Form 8-K of Jaguar Health, Inc. filed May 19, 2023, File No. 001-36714).</a>
10.84	<a href="#">Form of Exchange Agreement, dated June 28, 2023, by and between Jaguar Health, Inc. and Uptown Capital, LLC (incorporated by reference to Exhibit 10.1 to the Form 8-K filed July 3, 2023, File No. 001-36714).</a>
10.85	<a href="#">First Amendment to the Standstill Agreement, dated June 28, 2023 (incorporated by reference to Exhibit 10.2 to the Form 8-K of Jaguar Health, Inc. filed July 3, 2023, File No. 001-36714).</a>
10.86	<a href="#">Binding Memorandum of Understanding, dated June 30, 2023, by and among Jaguar Health, Inc., Napo Pharmaceuticals, Inc., Iliad Research and Trading, L.P., Uptown Capital, LLC and Streeterville Capital, LLC (incorporated by reference to Exhibit 10.6 to the Form 10-Q filed August 14, 2023, File No. 001-36714).</a>
10.87	<a href="#">Amendment No. 1 to Manufacturing and Supply Agreement, dated July 12, 2023, by and between Napo Pharmaceuticals, Inc. and Glenmark Life Sciences Limited (incorporated by reference to Exhibit 10.7 to the Form 10-Q filed August 14, 2023, File No. 001-36714).</a>
10.88	<a href="#">Exchange Agreement, dated September 29, 2023, by and between Jaguar Health, Inc. and Uptown Capital, LLC (incorporated by reference to Exhibit 10.1 to the Form 8-K filed October 5, 2023, File No. 001-36714).</a>

Exhibit No.	Description
10.89	<a href="#">First Amendment to 200 Pine Street Office Lease, dated December 24, 2021, between Jaguar Health, Inc. and M &amp; E, LLC (incorporated by reference to Exhibit 10.1 to the Form 8-K filed December 1, 2023, File No. 001-36714).</a>
10.90	<a href="#">Second Amendment to 200 Pine Street Office Lease, dated October 25, 2023, between Jaguar Health, Inc. and M &amp; E, LLC (incorporated by reference to Exhibit 10.2 to the Form 8-K filed December 1, 2023, File No. 001-36714).</a>
10.91	<a href="#">Exchange Agreement, dated March 1, 2024, by and between Jaguar Health, Inc. and Streeterville Capital, LLC (incorporated by reference to Exhibit 10.1 to the Form 8-K filed March 1, 2024, File No. 001-36714).</a>
10.92	<a href="#">Form of PIPE Warrant Exchange Agreement, dated February 27, 2024, by and between Jaguar Health, Inc. and the PIPE investor (incorporated by reference to Exhibit 10.2 to the Form 8-K filed March 1, 2024, File No. 001-36714).</a>
21.1*	<a href="#">Subsidiaries of the Registrant.</a>
23.1*	<a href="#">Consent of RBSM LLP, Independent Registered Public Accounting Firm.</a>
31.1*	<a href="#">Principal Executive Officer's Certifications Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.</a>
31.2*	<a href="#">Principal Financial Officer's Certifications Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.</a>
32.1**	<a href="#">Certification Pursuant to 18 U.S.C. § 1350 (Section 906 of Sarbanes-Oxley Act of 2002).</a>
32.2**	<a href="#">Certification Pursuant to 18 U.S.C. § 1350 (Section 906 of Sarbanes-Oxley Act of 2002).</a>
97*	<a href="#">Jaguar Health, Inc. Clawback Policy.</a>
101.INS	Inline XBRL Instance Document
101.SCH	Inline XBRL Taxonomy Extension Schema
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase
104	Cover Page Interactive Data File (formatted as inline XBRL and contained in Exhibit 101)

\* Filed herewith.

\*\* In accordance with Item 601(b)(32)(ii) of Regulation S-K and SEC Release No. 34-47986, the certifications furnished in Exhibits 32.1 and 32.2 hereto are deemed to accompany this Form 10-K and will not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934 (the "Exchange Act") or deemed to be incorporated by reference into any filing under the Exchange Act or the Securities Act of 1933 except to the extent that the registrant specifically incorporates it by reference.

† Confidential treatment granted as to portions of the exhibit. Confidential materials omitted and filed separately with the Securities and Exchange Commission.

‡ Management contract or compensatory plan or arrangement.

# Portions of this exhibit have been omitted pursuant to Item 601 of Regulation S-K promulgated under the Securities Act because the information (i) is not material and (ii) would be competitively harmful if publicly disclosed.

#### ITEM 16. FORM 10-K SUMMARY

None.

## SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

## JAGUAR HEALTH, INC.

By: \_\_\_\_\_ /s/ LISA A. CONTE

Lisa A. Conte

*Elisa A. Cente*  
*Chief Executive Officer and President*

## POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Lisa A. Conte and Carol Lizak, jointly and severally, his or her attorneys-in-fact, each with the power of substitution, for him or her in any and all capacities, to sign any amendments to this Annual Report on Form 10-K, and to file the same, with exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, hereby ratifying and confirming all that each of said attorneys-in-fact, or his or her substitute or substitutes, may do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933, this Registration Statement has been signed by the following persons in the capacities and on the date indicated.

Signature	Title	Date
<u>/s/ LISA A. CONTE</u>	Chief Executive Officer, President and Director (Principal Executive Officer)	April 1, 2024
Lisa A. Conte		
<u>/s/ CAROL LIZAK</u>	Chief Financial Officer and Treasurer (Principal Financial and Accounting Officer)	April 1, 2024
Carol Lizak		
<u>/s/ JAMES J. BOCHNOWSKI</u>	Chairman of the Board	April 1, 2024
James J. Bochnowski		
<u>/s/ JOHN MICEK III</u>	Director	April 1, 2024
John Micek III		
<u>/s/ JONATHAN B. SIEGEL</u>	Director	April 1, 2024
Jonathan B. Siegel		
<u>/s/ ANULA JAYASURIYA</u>	Director	April 1, 2024
Anula Jayasuriya		

SUBSIDIARIES OF JAGUAR HEALTH, INC.

Name of Subsidiary	State or Other Jurisdiction of Incorporation or Organization
Napo Pharmaceuticals, Inc.	Delaware
Napo Therapeutics S.p.A.	Italy

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101 Larkspur Landing Circle,  
Suite 321  
Larkspur, CA 94939

[www.rbsmllp.com](http://www.rbsmllp.com)

**CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM**

We consent to the incorporation by reference in the following Jaguar Health, Inc.'s Registrations Statements:

1. *Registration Statements on Form S-1 (File Nos. 333-236016, 333-232082, 333-231399, 333-232078, 333-232715, 333-233989 and No. 333-237587); and*
2. *Registration Statements on Form S-3 (File Nos. 333-238992, 333-248763, 333-220236, 333-255154, 333-256634 and 333-261283); and*
3. *Registration Statements on Form S-8 (File Nos. 333-204280, 333-215303, 333-219939, 333-225057, 333-237816, 333-256626, 333-256629, 333-264274, 333-264276, 333-271156, 333-271948, 333-273973).*

of our report dated April 1, 2024, with respect to our audits of the consolidated financial statements of Jaguar Health, Inc., as of December 31, 2023 and 2022 for each of the years in the two-year period ended December 31, 2023, which report is included in this Annual Report on Form 10-K of Jaguar Health, Inc., for the year ended December 31, 2023.

*/s/ RBSM LLP*

RBSM, LLP

Larkspur, California  
April 1, 2024

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**PRINCIPAL EXECUTIVE OFFICER'S CERTIFICATION PURSUANT TO  
SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002**

I, Lisa A. Conte, certify that:

1. I have reviewed this annual report on Form 10-K of Jaguar Health, Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
  - a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
  - b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
  - c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
  - d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
  - a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
  - b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: April 1, 2024

/s/ LISA A. CONTE

Lisa A. Conte

*Chief Executive Officer and President  
(Principal Executive Officer)*

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**PRINCIPAL FINANCIAL OFFICER'S CERTIFICATION PURSUANT TO  
SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002**

I, Carol Lizak, certify that:

1. I have reviewed this annual report on Form 10-K of Jaguar Health, Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
  - a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
  - b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
  - c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
  - d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
  - a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
  - b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: April 1, 2024

*/s/ CAROL LIZAK*  
Carol Lizak  
*Principal Financial and Accounting Officer*

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**CERTIFICATION PURSUANT TO  
18 U.S.C. SECTION 1350,  
AS ADOPTED PURSUANT TO  
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

In connection with the annual report of Jaguar Health, Inc. (the "Company") on Form 10-K for the year ended December 31, 2023, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned officer of the Company certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, to such officer's knowledge:

- (1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
- (2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: April 1, 2024

*/s/ LISA A. CONTE*  
Lisa A. Conte  
*Chief Executive Officer and President*  
*(Principal Executive Officer)*

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**CERTIFICATION PURSUANT TO  
18 U.S.C. SECTION 1350,  
AS ADOPTED PURSUANT TO  
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

In connection with the annual report of Jaguar Health, Inc. (the "Company") on Form 10-K for the year ended December 31, 2023, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned officer of the Company certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, to such officer's knowledge:

- (1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
- (2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: April 1, 2024

/s/ CAROL LIZAK  
Carol. Lizak  
*Principal Financial and Accounting Officer*

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**CLAWBACK POLICY**  
Adopted: November 7, 2023

**Purpose**

Jaguar Health, Inc. (the "Company") is establishing this policy to align the interests of executive officers of the Company with those of shareholders, to create and maintain a culture that emphasizes integrity and accountability and to enforce the Company's pay-for-performance compensation philosophy. This policy provides for the recoupment of certain executive compensation in the event of an accounting restatement resulting from material noncompliance with financial reporting requirements under the federal securities laws (the "Policy"). This Policy is designed to comply with Section 10D of the Securities Exchange Act of 1934 (the "Exchange Act"), Rule 10D-1 promulgated under the Exchange Act ("Rule 10D-1"), and Nasdaq Listing Rule 5608 (the "Listing Standards").

**Administration**

This Policy shall be administered by the Board of Directors (the "Board") of the Company or, if so designated by the Board, a committee thereof including the Compensation Committee, in which case references herein to the Board shall be deemed references to such committee. The Board is authorized to interpret and construe this Policy and to make all determinations and rules as it deems to be necessary or advisable for its administration. It is intended that this Policy be interpreted in a manner that is consistent with the requirements of Section 10D of the Exchange Act and any applicable rules or standards adopted by the Securities and Exchange Commission or the Nasdaq Stock Market ("Nasdaq"). Any determinations made by the Board shall be final and binding on all affected individuals. The Board may delegate administrative duties with respect to this Policy to one or more directors or employees of the Company, as permitted under applicable law, including any Listing Standards.

**Covered Executives**

This Policy applies to the Company's current and former executive officers, as determined by the Board in accordance with Section 10D of the Exchange Act, the definition of executive officer set forth in Rule 10D-1 and the Listing Standards ("Covered Executives"), and such other employees who may from time to time be deemed subject to the Policy by the Board. For this purpose, an "executive officer" includes the Company's president, principal financial officer, principal accounting officer (or controller), any vice president in charge of a principal business unit, division or function or any other officer or person who performs a "policy-making" function for the Company.

**Recoupment; Accounting Restatement**

In the event that the Company is required to prepare an Accounting Restatement, as defined herein, the Board will promptly require reimbursement or forfeiture of any Excess Incentive Compensation, as defined herein, received by any Covered Executive during the three completed fiscal years immediately preceding the date on which the Company is required to prepare an Accounting Restatement, and including any transition period (that results from a change in the Company's fiscal year) within or immediately following those three completed fiscal years, except

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that a transition period comprising a period of at least nine months shall count as a full fiscal year. The Policy applies to all Incentive-Based Compensation received by a Covered Executive (i) after beginning service as an executive officer; (ii) who served as an executive officer at any time during the performance period for that Incentive-Based Compensation; and (iii) while the Company has a listed class of securities. Recovery of amounts under this Policy with respect to a Covered Executive shall not require the finding of any misconduct by such Covered Executive or that such Covered Executive caused or contributed to any error associated with an Accounting Restatement. For clarity, the recovery of any executive compensation under this Policy will not give rise to any person's right to voluntarily terminate employment for "good reason," or due to a "constructive termination" (or any similar term of like effect) under any plan, program or policy of or agreement with the Company or any of its affiliates.

For purposes of this Policy, an "**Accounting Restatement**" means an accounting restatement of the Company's financial statements due to the Company's material noncompliance with any financial reporting requirement under the securities laws, including any required accounting restatement to correct an error in previously issued financial statements that is material to the previously issued financial statements, or that would result in a material misstatement if the error were corrected in the current period or left uncorrected in the current period. Also for purposes of this Policy, the date on which the Company is required to prepare an accounting restatement is the earlier of (i) the date the Board concludes, or reasonably should have concluded, that the Company is required to prepare an Accounting Restatement; or (ii) the date a court, regulator, or other legally authorized body directs the Company to prepare an Accounting Restatement, in each case regardless of whether or when the restated financial statements are filed.

#### **Excess Incentive Compensation: Amount Subject to Recovery**

The amount subject to recovery (the "**Excess Incentive Compensation**") is the excess of the Incentive-Based Compensation paid to the Covered Executive based on the erroneous data over the Incentive-Based Compensation that would have been paid to the Covered Executive had it been based on the restated results. Excess Incentive Compensation shall be determined by the Board without regard to any taxes paid by the Covered Executive with respect to the Excess Incentive Compensation.

For Incentive-Based Compensation based on stock price or total shareholder return: (i) the Board shall determine the amount of the Excess Incentive Compensation based on a reasonable estimate of the effect of the Accounting Restatement on the stock price or total shareholder return upon which the Incentive-Based Compensation was received; and (ii) the Company shall maintain documentation of the determination of that reasonable estimate and provide such documentation to Nasdaq.

**"Incentive-Based Compensation"** means any compensation that is granted, earned, or vested based wholly or in part upon the attainment of a Financial Reporting Measure. Incentive-Based Compensation is received for purposes of this Policy in the Company's fiscal period during which the Financial Reporting Measure specified in the Incentive-Based Compensation award is attained, even if the payment or grant of the Incentive-Based Compensation occurs after the end of that period.

A “**Financial Reporting Measure**” means any measure that is determined and presented in accordance with the accounting principles used in preparing the Company’s financial statements, and any measure that is derived in whole or in part from such measure. For purposes of this Policy, Financial Reporting Measures include, but are not limited to, the following, and any measures derived from the following: revenues; earnings before interest, taxes, depreciation and amortization; net income; Company stock price; and total shareholder return. A Financial Reporting Measure need not be presented within the Company’s financial statements or included in a filing with the Securities Exchange Commission.

#### **Method of Recoupment**

The Board shall determine, in its sole discretion, the timing and method for promptly recouping Excess Incentive Compensation, which may include without limitation:

- (a) seeking reimbursement of all or part of any cash or equity Incentive-Based Compensation previously paid,
- (b) seeking recovery of any gain realized on the vesting, exercise, settlement, sale, transfer, or other disposition of any equity-based awards,
- (c) cancelling prior cash or equity-based awards, whether vested or unvested or paid or unpaid,
- (d) cancelling or offsetting against any planned future cash or equity-based awards,
- (e) forfeiture of deferred compensation, subject to compliance with Section 409A of the Internal Revenue Code (the “**Code**”) and the regulations promulgated thereunder, and
- (f) any other method authorized by applicable law or contract.

Subject to compliance with any applicable law, the Board may recover amounts under this Policy from any amount otherwise payable to the Covered Executive.

The Company is authorized and directed pursuant to this Policy to recoup Excess Incentive Compensation in compliance with this Policy unless the Compensation Committee of the Board has determined that recovery would be impracticable solely for the following limited reasons, and subject to the following procedural and disclosure requirements:

- The direct expense paid to a third party to assist in enforcing the Policy would exceed the amount to be recovered; provided that prior to concluding that it would be impracticable to recover any amount of Excess Incentive Compensation based on expense of enforcement, the Board must make a reasonable attempt to recover such erroneously awarded compensation, document such reasonable attempt(s) to recover and provide that documentation to Nasdaq; or
- Recovery would likely cause an otherwise tax-qualified retirement plan, under which benefits are broadly available to employees of the Company, to fail to meet the requirements of 26 U.S.C. 401(a)(13) or 26 U.S.C. 411(a) and regulations thereunder.

## **No Indemnification of Covered Executives; No Liability**

The Company shall not indemnify any Covered Executives against the loss of any incorrectly awarded Excess Incentive Compensation. The Company is prohibited from paying or reimbursing a Covered Executive for purchasing insurance to cover any such loss. None of the Company, an affiliate of the Company or any member of the Board shall have any liability to any person as a result of actions taken under this Policy.

## **Board Indemnification**

Any members of the Board or its delegates shall not be personally liable for any action, determination or interpretation made with respect to this Policy and shall be fully indemnified by the Company to the fullest extent under applicable law and Company organizational documents and policy with respect to any such action, determination or interpretation. The foregoing sentence shall not limit any other rights to indemnification of the members of the Board or its delegates under applicable law or Company organizational documents and policy.

## **Effective Date**

This Policy shall be effective as of the effective date of the Listing Standards (the **Effective Date**). The terms of this Policy shall apply to any Incentive-Based Compensation that is received by Covered Executives on or after the Effective Date, even if such Incentive-Based Compensation was approved, awarded, granted or paid to Covered Executives prior to the Effective Date.

## **Amendment and Termination**

The Board may amend this Policy from time to time in its discretion and shall amend this Policy as it deems necessary to reflect final regulations adopted by the Securities and Exchange Commission under Section 10D of the Exchange Act, to comply with any rules or standards adopted by Nasdaq, and to comply with (or maintain an exemption from the application of) Section 409A of the Code. The Board may terminate this Policy at any time. This Policy will terminate automatically when the Company does not have a class of securities listed on a national securities exchange or association.

## **Other Recoupment Rights**

The Board intends that this Policy will be applied to the fullest extent of the law. The Board may require that any employment agreement, equity award agreement, or similar agreement entered into on or after the Effective Date shall, as a condition to the grant of any benefit thereunder, require a Covered Executive to agree to abide by the terms of this Policy. Any right of recoupment under this Policy is in addition to, and not in lieu of, any other remedies or rights of recoupment that may be available to the Company pursuant to the terms of any similar policy in any employment agreement, equity award agreement, or similar agreement and any other legal remedies available to the Company.

## **Severability**

The provisions in this Policy are intended to be applied to the fullest extent of the law. To the extent that any provision of this Policy is found to be unenforceable or invalid under any applicable law, such provision shall be applied to the maximum extent permitted, and shall automatically be deemed amended in a manner consistent with its objectives to the extent necessary to conform to any limitations required under applicable law.

## **Governing Law**

This Policy and all rights and obligations hereunder are governed by and construed in accordance with the internal laws of the State of Delaware, excluding any choice of law rules or principles that may direct the application of the laws of another jurisdiction.

## **Successors**

This Policy shall be binding and enforceable against all Covered Executives and their beneficiaries, heirs, executors, administrators or other legal representatives.

## **Exhibit Filing Requirement**

A copy of this Policy and any amendments thereto shall be filed as an exhibit to the Company's annual report on Form 10-K.

[FOR SIGNATURE BY THE COMPANY'S COVERED EXECUTIVES]

Clawback Policy Acknowledgment

I, the undersigned, agree and acknowledge that I am fully bound by, and subject to, all of the terms and conditions of the Jaguar Health, Inc. Clawback Policy (as may be amended, restated, supplemented or otherwise modified from time to time, the "Policy"). In the event of any inconsistency between the Policy and the terms of any employment agreement to which I am a party, or the terms of any compensation plan, program or agreement under which any compensation has been granted, awarded, earned or paid, the terms of the Policy shall govern. In the event it is determined by the Board, or such committee thereof that is charged with administration of the Policy, that any amounts granted, awarded, earned or paid to me must be forfeited or reimbursed to the Company, I will promptly take any action necessary to effectuate such forfeiture and/or reimbursement. Any capitalized terms used in this Acknowledgment without definition shall have the meaning set forth in the Policy.

By:   
Name: Carol Lizak  
Title: CFO

Date: Nov 28, 2023