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DELTA REPORT

10-Q

DNLI - DENALI THERAPEUTICS INC.

10-Q - MARCH 31, 2024 COMPARED TO 10-Q - SEPTEMBER 30, 2023

The following comparison report has been automatically generated

TOTAL DELTAS	1898
CHANGES	161
DELETIONS	823
ADDITIONS	914

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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 10-Q

(Mark One)

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

For the quarterly period ended September 30, 2023 March 31, 2024

OR

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

For the transition period from _____ to _____

Commission File Number: 001-38311

Denali Therapeutics Inc.

(Exact name of registrant as specified in its charter)

Delaware	**46-3872213**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**

161 Oyster Point Blvd.
South San Francisco, CA, 94080

(Address of principal executive offices and zip code)

(650) 866-8548
(Registrant's telephone number, including area code)

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol	Name of each exchange on which registered
Common Stock, par value $0.01 per share	DNLI	Nasdaq Global Select Market

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 (§232.405 of this chapter) 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 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 is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ☐ No ☒

The number of outstanding shares of the registrant's common stock as of October 30, 2023 April 30, 2024 was 138,196,848. 142,609,036. This number does not include 26,046,065 shares of common stock issuable upon the exercise of pre-funded warrants outstanding as of April 30, 2024 (which are immediately exercisable at an exercise price of $0.01 per share of common stock, subject to beneficial ownership limitations) sold in the registrant's private placement in February 2024. See Note 7 — Common Stock to the registrant's condensed consolidated financial statements.

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PART I. FINANCIAL INFORMATION

ITEM 1. FINANCIAL STATEMENTS

Denali Therapeutics Inc.

Condensed Consolidated Balance Sheets
(Unaudited)
(In thousands, except share amounts)

		September 30, 2023	December 31, 2022			
	March 31, 2024				**March 31, 2024**	**December 31, 2023**
Assets	**Assets**					
Current assets:	Current assets:					
Current assets:						
Current assets:						
Cash and cash equivalents						
Cash and cash equivalents						
Cash and cash equivalents	Cash and cash equivalents	$ 148,011	$ 218,044			
Short-term marketable securities	Short-term marketable securities	961,245	1,118,171			

Prepaid expenses and other current assets	Prepaid expenses and other current assets	33,628	36,104
Total current assets	Total current assets	1,142,884	1,372,319
Long-term marketable securities	Long-term marketable securities	7,905	—
Property and equipment, net	Property and equipment, net	48,101	44,087
Operating lease right-of-use assets		26,750	30,437
Operating lease right-of-use asset			
Other non-current assets			
Other non-current assets			
Other non-current assets	Other non-current assets	11,137	13,399
Total assets	Total assets	$1,236,777	$1,460,242
Liabilities and stockholders' equity	**Liabilities and stockholders' equity**		
Current liabilities:	Current liabilities:		
Current liabilities:			
Current liabilities:			
Accounts payable	Accounts payable	$ 1,182	$ 2,790
Cost sharing payments due to related party		10,354	4,388
Accounts payable			
Accounts payable			
Accrued clinical and other research & development costs	Accrued clinical and other research & development costs	14,534	16,297
Accrued manufacturing costs	Accrued manufacturing costs	12,421	22,307
Other accrued costs and current liabilities	Other accrued costs and current liabilities	9,331	3,682
Accrued compensation	Accrued compensation	16,344	17,087
Operating lease liabilities, current		7,014	7,318
Related-party contract liability, current		—	290,053
Operating lease liability, current			
Deferred research funding liability, current			
Total current liabilities	Total current liabilities	71,180	363,922
Related-party contract liability, less current portion		—	479
Total current liabilities			
Total current liabilities			

Operating lease liabilities, less current portion		46,887	53,032
Other non-current liabilities		379	379
Operating lease liability, less current portion			
Operating lease liability, less current portion			
Operating lease liability, less current portion			
Total liabilities	Total liabilities	118,446	417,812
Commitments and contingencies (Note 7)			
Total liabilities			
Total liabilities			
Commitments and contingencies (Note 6)			
			Commitments and contingencies (Note 6)
Stockholders' equity:	Stockholders' equity:		
Convertible preferred stock, $0.01 par value; 40,000,000 shares authorized as of September 30, 2023 and December 31, 2022; 0 shares issued and outstanding as of September 30, 2023 and December 31, 2022		—	—
Common stock, $0.01 par value; 400,000,000 shares authorized as of September 30, 2023 and December 31, 2022; 138,051,798 shares and 135,965,918 shares issued and outstanding as of September 30, 2023 and December 31, 2022, respectively		1,707	1,686
Convertible preferred stock, $0.01 par value; 40,000,000 shares authorized as of March 31, 2024 and December 31, 2023; 0 shares issued and outstanding as of March 31, 2024 and December 31, 2023			
Convertible preferred stock, $0.01 par value; 40,000,000 shares authorized as of March 31, 2024 and December 31, 2023; 0 shares issued and outstanding as of March 31, 2024 and December 31, 2023			
Convertible preferred stock, $0.01 par value; 40,000,000 shares authorized as of March 31, 2024 and December 31, 2023; 0 shares issued and outstanding as of March 31, 2024 and December 31, 2023			
Common stock, $0.01 par value; 400,000,000 shares authorized as of March 31, 2024 and December 31, 2023; 142,512,856 shares and 138,385,498 shares issued and outstanding as of March 31, 2024 and December 31, 2023, respectively			
Additional paid-in capital	Additional paid-in capital	2,114,013	2,018,617
Accumulated other comprehensive loss		(651)	(6,886)

Accumulated other comprehensive income (loss)			
Accumulated deficit	Accumulated deficit	(996,738)	(970,987)
Total stockholders' equity	Total stockholders' equity	1,118,331	1,042,430
Total liabilities and stockholders' equity	Total liabilities and stockholders' equity	$1,236,777	$1,460,242

See accompanying notes to unaudited condensed consolidated financial statements.

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Denali Therapeutics Inc.

Condensed Consolidated Statements of Operations and Comprehensive Loss
(Unaudited)
(In thousands, except share and per share amounts)

		Three Months Ended September 30,		Nine Months Ended September 30,	
		2023	2022	2023	2022
		Three Months Ended March 31,	Three Months Ended March 31,	Three Months Ended March 31,	
		2024			
Collaboration revenue:	Collaboration revenue:				
Collaboration revenue from customers(1)	Collaboration revenue from customers(1)	$ 1,267	$ 184	$ 330,531	$ 94,805
Other collaboration revenue		—	3,375	—	3,375
Collaboration revenue from customers(1)	Collaboration revenue from customers(1)				
Total collaboration revenue	Total collaboration revenue				
Total collaboration revenue	Total collaboration revenue	1,267	3,559	330,531	98,180
Operating expenses:	Operating expenses:				
Research and development(2)	Research and development(2)	89,737	87,786	316,073	266,621
Research and development(2)	Research and development(2)				

General and administrative	General and administrative	25,325	23,259	78,585	66,959
Total operating expenses	Total operating expenses	115,062	111,045	394,658	333,580
Total operating expenses					
Total operating expenses					
Gain from divestiture of small molecule programs					
Loss from operations	Loss from operations	(113,795)	(107,486)	(64,127)	(235,400)
Interest and other income, net	Interest and other income, net	14,442	4,187	38,376	8,114
Loss before income taxes		(99,353)	(103,299)	(25,751)	(227,286)
Income tax expense		—	—	—	(27)
Net loss					
Net loss					
Net loss	Net loss	(99,353)	(103,299)	(25,751)	(227,313)
Other comprehensive income (loss):	Other comprehensive income (loss):				
Net unrealized gain (loss) on marketable securities, net of tax					
Net unrealized gain (loss) on marketable securities, net of tax					
Net unrealized gain (loss) on marketable securities, net of tax	Net unrealized gain (loss) on marketable securities, net of tax	790	421	6,235	(9,354)
Comprehensive loss	Comprehensive loss	$ (98,563)	$ (102,878)	$ (19,516)	$ (236,667)
Net loss per share, basic and diluted	Net loss per share, basic and diluted	$ (0.72)	$ (0.84)	$ (0.19)	$ (1.85)
Weighted average number of shares outstanding, basic and diluted	Weighted average number of shares outstanding, basic and diluted	137,644,534	123,473,390	137,076,199	123,054,889
Weighted average number of shares outstanding, basic and diluted					
Weighted average number of shares outstanding, basic and diluted				149,404,188	136,524,528

(1) Includes related-party collaboration revenue from customers of $1.3 million and $295.5 $0.1 million for the three and nine months ended September 30, 2023, respectively, and $0.2 million and $2.9 million for the three and nine months ended September 30, 2022, respectively. March 31, 2023.

(2) Includes expenses for cost sharing payments due to a related party of $3.4 million and $14.5 $4.2 million for the three and nine months ended September 30, 2023, respectively, and $1.4 million and $3.8 million for the three and nine months ended September 30, 2022 March 31, 2023.

See accompanying notes to unaudited condensed consolidated financial statements.

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Denali Therapeutics Inc.

Condensed Consolidated Statements of Stockholders' Equity
(Unaudited)
(In thousands, except share amounts)

		Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total Stockholders' Equity
		Common Stock					
		Common Stock					
	Shares						
Balance at December 31, 2022							
Balance at December 31, 2022							
		Common Stock		Additional Paid-in	Accumulated Other Comprehensive	Accumulated	Total Stockholders'
		Shares	Amount	Capital	Loss	Deficit	Equity
Balance at December 31, 2022	Balance at December 31, 2022	135,965,918	$ 1,686	$ 2,018,617	$ (6,886)	$ (970,987)	$ 1,042,430
Issuances under equity incentive plans	Issuances under equity incentive plans	953,575	9	13,106	—	—	13,115
Vesting of restricted stock units	Vesting of restricted stock units	1,132,305	12	(12)	—	—	—
Stock-based compensation	Stock-based compensation	—	—	82,302	—	—	82,302
Net loss	Net loss	—	—	—	—	(25,751)	(25,751)
Other comprehensive income	Other comprehensive income	—	—	—	6,235	—	6,235
Balance at September 30, 2023		138,051,798	$ 1,707	$ 2,114,013	$ (651)	$ (996,738)	$ 1,118,331
Balance at March 31, 2023							
Balance at June 30, 2023		137,362,688	$ 1,700	$ 2,083,951	$ (1,441)	$ (897,385)	$ 1,186,825
Balance at December 31, 2023							
Balance at December 31, 2023							
Balance at December 31, 2023							
Issuance of common stock and pre-funded warrants, net of issuance costs of $480K							
Issuances under equity incentive plans	Issuances under equity incentive plans	222,688	2	2,490	—	—	2,492
Vesting of restricted stock units		466,422	5	(5)	—	—	—
Stock-based compensation		—	—	27,577	—	—	27,577
Net loss		—	—	—	—	(99,353)	(99,353)
Other comprehensive income		—	—	—	790	—	790
Balance at September 30, 2023		138,051,798	$ 1,707	$ 2,114,013	$ (651)	$ (996,738)	$ 1,118,331
Balance at December 31, 2021		122,283,305	$ 1,548	$ 1,608,238	$ (2,499)	$ (644,996)	$ 962,291
Issuances under equity incentive plans							
Issuances under equity incentive plans	Issuances under equity incentive plans	723,604	8	11,011	—	—	11,019
Vesting of restricted stock units	Vesting of restricted stock units	789,529	8	(8)	—	—	—
Stock-based compensation	Stock-based compensation	—	—	74,660	—	—	74,660
Net loss	Net loss	—	—	—	—	(227,313)	(227,313)
Other comprehensive loss	Other comprehensive loss	—	—	—	(9,354)	—	(9,354)
Balance at September 30, 2022		123,796,438	$ 1,564	$ 1,693,901	$ (11,853)	$ (872,309)	$ 811,303
Balance at June 30, 2022		123,157,278	$ 1,558	$ 1,664,174	$ (12,274)	$ (769,010)	$ 884,448

Issuances under equity incentive plans	331,643	3	5,151	—	—	5,154
Vesting of restricted stock units	307,517	3	(3)	—	—	—
Stock-based compensation	—	—	24,579	—	—	24,579
Net loss	—	—	—	—	(103,299)	(103,299)
Other comprehensive income	—	—	—	421	—	421
Balance at September 30, 2022	123,796,438	$ 1,564	$ 1,693,901	$ (11,853)	$ (872,309)	$ 811,303
Balance at March 31, 2024						

See accompanying notes to unaudited condensed consolidated financial statements.

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Denali Therapeutics Inc.

Condensed Consolidated Statements of Cash Flows
(Unaudited)
(In thousands)

	Nine Months Ended September 30,	
	2023	2022
Operating activities		
Net loss	$ (25,751)	$(227,313)
Net loss		
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization		
Depreciation and amortization	14,549	6,292
Stock–based compensation expense	82,114	74,660
Net amortization of premiums and (discounts) on marketable securities	(31,709)	1,430
Non-cash adjustment to operating lease expense	(2,762)	(2,488)
Other non-cash items	—	51
Non-cash gain from divestiture of small molecule programs		

	Three Months Ended March 31,	
	2024	2023
Operating activities		
Net loss		
Net loss		
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization		
Depreciation and amortization		
Stock–based compensation expense		
Net amortization of premiums and (discounts) on marketable securities		
Non-cash adjustment to operating lease expense		
Other non-cash items		
Non-cash gain from divestiture of small molecule programs		

Non-cash gain from divestiture of small molecule programs			
Non-cash gain from divestiture of small molecule programs			
Changes in operating assets and liabilities:	Changes in operating assets and liabilities:		
Prepaid expenses and other assets			
Prepaid expenses and other assets			
Prepaid expenses and other assets	Prepaid expenses and other assets	1,910	(1,386)
Accounts payable	Accounts payable	4,512	3,989
Accruals and other current liabilities	Accruals and other current liabilities	(11,665)	6,891
Contract liabilities		—	(31,290)
Related-party contract liability			
Related-party contract liability			
Related-party contract liability	Related-party contract liability	(290,532)	(2,889)
Net cash used in operating activities	Net cash used in operating activities	(259,334)	(172,053)
Net cash used in operating activities			
Net cash used in operating activities			
Investing activities	**Investing activities**		
Purchases of marketable securities			
Purchases of marketable securities			
Purchases of marketable securities	Purchases of marketable securities	(1,399,982)	(628,330)
Purchases of property and equipment	Purchases of property and equipment	(10,704)	(12,984)
Maturities and sales of marketable securities	Maturities and sales of marketable securities	1,586,947	627,486
Net cash provided by (used in) investing activities		176,261	(13,828)
Net cash used in investing activities			
Net cash used in investing activities			
Net cash used in investing activities			

Financing activities	**Financing activities**		
Proceeds from issuance of common stock and pre-funded warrants, net of issuance costs of $480K			
Proceeds from issuance of common stock and pre-funded warrants, net of issuance costs of $480K			
Proceeds from issuance of common stock and pre-funded warrants, net of issuance costs of $480K			
Proceeds from exercise of awards under equity incentive plans			
Proceeds from exercise of awards under equity incentive plans			
Proceeds from exercise of awards under equity incentive plans	Proceeds from exercise of awards under equity incentive plans	13,115	11,019
Net cash provided by financing activities	Net cash provided by financing activities	13,115	11,019
Net decrease in cash, cash equivalents and restricted cash	Net decrease in cash, cash equivalents and restricted cash	(69,958)	(174,862)
Cash, cash equivalents and restricted cash at beginning of period	Cash, cash equivalents and restricted cash at beginning of period	219,544	294,977
Cash, cash equivalents and restricted cash at end of period	Cash, cash equivalents and restricted cash at end of period	$ 149,586	$ 120,115
Supplemental disclosures of cash flow information	**Supplemental disclosures of cash flow information**		
Cash paid during the period for income taxes	Cash paid during the period for income taxes	$ 4	$ —
Cash paid during the period for income taxes			
Cash paid during the period for income taxes			
Equity consideration received in the divestiture of small molecule programs (Note 10)			

Property and equipment purchases accrued but not yet paid	Property and equipment purchases accrued but not yet paid	$ 6,230	$ 284
Issuance costs incurred but not yet paid			
Issuance costs incurred but not yet paid			
Issuance costs incurred but not yet paid			

See accompanying notes to unaudited condensed consolidated financial statements.

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Denali Therapeutics Inc.
Notes to Condensed Consolidated Financial Statements
(Unaudited)

1. Significant Accounting Policies

Organization and Description of Business

Denali Therapeutics Inc. ("Denali" or the "Company") is a biopharmaceutical company, incorporated in Delaware, that discovers and develops therapeutics to defeat neurodegenerative diseases. The Company is headquartered in South San Francisco, California.

Basis of Presentation

The accompanying unaudited condensed consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America ("U.S. GAAP") for interim financial information and the instructions to Form 10-Q and Article 10 of the Securities and Exchange Commission ("SEC") Regulation S-X for interim financial information.

These unaudited condensed consolidated financial statements and notes should be read in conjunction with the audited consolidated financial statements and notes thereto contained in the Annual Report on Form 10-K for the year ended December 31, 2022 December 31, 2023, as filed with the SEC on February 27, 2023 February 28, 2024 (the "2022 "2023 Annual Report on Form 10-K"). The Condensed Consolidated Balance Sheet as of December 31, 2022 December 31, 2023 was derived from the audited annual consolidated financial statements as of and for the period then ended. Certain information and footnote disclosures typically included in the Company's annual consolidated financial statements have been condensed or omitted. The accompanying unaudited condensed consolidated financial statements reflect all adjustments that, in the opinion of management, are necessary for a fair statement of the results of the interim periods presented. All such adjustments are of a normal recurring nature except for the impacts of adopting new accounting standards, if any, discussed below. These interim financial results are not necessarily indicative of results expected for the full fiscal year or for any subsequent interim period.

During the nine three months ended September 30, 2023 March 31, 2024 there were no material changes to the Company's significant accounting and financial reporting policies from those reflected in the 2022 2023 Annual Report on Form 10-K. For further information with regard to the Company's Significant Accounting Policies, please refer to Note 1, "Significant Accounting Policies," to the Company's Consolidated Financial Statements included in the 2022 2023 Annual Report on Form 10-K.

Principles of Consolidation

These unaudited condensed consolidated financial statements include the accounts of the Company and its wholly-owned subsidiaries. All intercompany balances and transactions have been eliminated in consolidation. For the Company and its subsidiaries, the functional currency has been determined to be U.S. dollars. Monetary assets and liabilities denominated in foreign currency are remeasured at period-end exchange rates, non-monetary assets and liabilities denominated in foreign currencies are remeasured at historical rates, and transactions in foreign currencies are remeasured at average exchange rates. Foreign currency gains and losses resulting from remeasurement are recognized in interest and other income, net in the Condensed Consolidated Statements of Operations and Comprehensive Loss.

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Use of Estimates

The preparation of financial statements in conformity with U.S. GAAP requires the Company to make certain estimates, judgments and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the condensed consolidated financial statements, as well as the reported amounts of expenses during the reporting period. Actual results could differ from those estimates, and such differences could be material to the Condensed Consolidated Balance Sheets and Condensed Consolidated Statements of Operations and Comprehensive Loss.

Concentration of Credit Risk and Other Risks and Uncertainties

Financial instruments that potentially subject the Company to significant concentrations of credit risk consist primarily of cash, cash equivalents, and marketable securities. Substantially all of the Company's cash and cash equivalents are deposited in accounts with financial institutions that management believes are of high credit quality. Such deposits have and will continue to exceed federally insured limits. The Company maintains its cash with accredited financial institutions and accordingly, such funds are subject to minimal credit risk.

The Company's investment policy limits investments to certain types of securities issued by the U.S. government and its agencies, as well as institutions with investment-grade credit ratings and places restrictions on maturities and concentration by type and issuer. The Company is exposed to credit risk in the event of a default by the financial institutions holding its cash, cash equivalents and marketable securities and issuers of marketable securities to the extent recorded on the Condensed Consolidated Balance Sheets. As of September 30, 2023 March 31, 2024 and December 31, 2022 December 31, 2023, the Company had no off-balance sheet concentrations of credit risk.

The Company is subject to a number of risks similar to other clinical-stage biopharmaceutical companies, including, but not limited to, the need to obtain adequate additional funding, possible failure of current or future preclinical testing or clinical trials, its reliance on third parties to conduct its clinical trials, the need to obtain regulatory and marketing approvals for its product candidates, competitors developing new technological innovations, the need to successfully commercialize and gain market acceptance of the Company's product candidates, its right to develop and commercialize its product candidates pursuant to the terms and conditions of the licenses granted to the Company, protection of proprietary technology, the ability to make milestone, royalty or other payments due under any license or collaboration agreements, and the need to secure and maintain adequate manufacturing arrangements with third parties. If the Company does not successfully commercialize or partner any of its product candidates, it will be unable to generate product revenue or achieve profitability. Further, the company is also subject to broad market risks and uncertainties resulting from recent events, such as bank failures or instability in the financial services sector, the COVID-19 pandemic, the Russian invasion of Ukraine, global pandemics, war and armed conflicts, inflation, rising interest rates, and recession risks as well as supply chain and labor shortages.

Segments

The Company has one operating segment. The Company's chief operating decision maker, its Chief Executive Officer, manages the Company's operations on a consolidated basis for the purposes of allocating resources.

Investments

Investments in equity securities may be accounted for using (i) the fair value option, if elected, (ii) fair value through earnings if fair value is readily determinable or (iii) for equity investments without readily determinable fair values, the measurement alternative to measure at cost adjusted for any impairment and observable price changes, as applicable. The election to use the measurement alternative is made for each eligible investment.

Cash, Cash Equivalents and Restricted Cash

The Company considers all highly liquid investments with original maturities of 90 days or less at the date of purchase to be cash and cash equivalents. Cash equivalents are reported at fair value.

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Cash, cash equivalents, and restricted cash reported within the Condensed Consolidated Statements of Cash Flows is composed of cash and cash equivalents reported in the Condensed Consolidated Balance Sheets and $1.6 million of restricted cash for the letter of credit for the Company's headquarters building lease which is included within other non-current assets in the Condensed Consolidated Balance Sheets. Sheets at March 31, 2024 and December 31, 2023.

Marketable Securities

The Company generally invests its excess cash in money market funds and investment grade short to intermediate-term fixed income securities. Such investments are included in cash and cash equivalents, or short-term marketable securities on the Condensed Consolidated Balance Sheets, are considered available-for-sale, and are reported at fair value with net unrealized gains and losses included as a component of stockholders' equity.

The Company classifies investments in securities with remaining maturities of less than one year, or where its intent is to use the investments to fund current operations or to make them available for current operations, as short-term investments. The Company classifies investments in securities with remaining maturities of over one year as long-term investments, unless intended to fund current operations. The amortized cost of debt securities is adjusted for amortization of premiums and accretion of discounts to maturity, which

is included in interest and other income, net in the Condensed Consolidated Statements of Operations and Comprehensive Loss. Realized gains and losses and declines in value determined to be due to credit losses on marketable securities, if any, are included in interest and other income, net.

The Company periodically evaluates the need for an allowance for credit losses. This evaluation includes consideration of several qualitative and quantitative factors, including whether it has plans to sell the security, whether it is more likely than not it will be required to sell any marketable securities before recovery of its amortized cost basis, and if the entity has the ability and intent to hold the security to maturity, and the portion of any unrealized loss that is the result of a credit loss. Factors considered in making these evaluations include quoted market prices, recent financial results and operating trends, implied values from any recent transactions or offers of investee securities, credit quality of debt instrument issuers, expected cash flows from securities, other publicly available information that may affect the value of the marketable security, duration and severity of the decline in value, and the Company's strategy and intentions for holding the marketable security.

Accounts Receivable

Accounts receivable are included within prepaid expenses and other current assets on the Condensed Consolidated Balance Sheets. The accounts receivable balance represents amounts receivable from the Company's collaboration partners, excluding related parties, net of an allowance for credit losses, if required.

Leases

The Company leases real estate and certain equipment for use in its operations. A determination is made as to whether an arrangement is a lease at inception. Right-of-use ("ROU") assets and operating lease liabilities are recognized for identified operating leases in the Condensed Consolidated Balance Sheets. The changes in operating lease ROU assets and operating lease liabilities are presented net within non-cash adjustment to operating lease expense in the Condensed Consolidated Statements of Cash Flows.

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ROU assets represent the Company's right to use the underlying asset for the lease term and lease liabilities represent the Company's obligation to make lease payments arising from the lease. Operating lease ROU assets and liabilities are recognized at the lease commencement date based on the present value of lease payments due over the lease term, with the ROU assets adjusted for lease incentives received. When determining the present value of lease payments, the Company uses its incremental borrowing rate on the date of lease commencement, or the rate implicit in the lease, if known. The Company does not assume renewals in its determination of the lease term unless the renewals are deemed by management to be reasonably certain at lease inception.

Leases with an initial term of twelve months or less are not recorded on the balance sheet, unless they include an option to purchase the underlying asset that the Company is reasonably certain to exercise. The Company recognizes lease expenses on a straight-line basis over the lease term. The Company has leases with lease and non-lease components, which the Company has elected to account for as a single lease component.

Revenue Recognition

License, Option and Collaboration Revenue

The Company analyzes its collaboration arrangements to assess whether they are within the scope of ASC 808, Collaborative Arrangements ("ASC 808") to determine whether such arrangements involve joint operating activities performed by parties that are both active participants in the activities and exposed to significant risks and rewards dependent on the commercial success of such activities. This assessment is performed throughout the life of the arrangement based on changes in the responsibilities of all parties in the arrangement. For collaboration arrangements within the scope of ASC 808 that contain multiple elements, the Company first determines which elements of the collaboration are deemed to be within the scope of ASC 808 and those that are more reflective of a vendor-customer relationship and, therefore, within the scope of Topic 606. For elements of collaboration arrangements that are accounted for pursuant to ASC 808, an appropriate recognition method is determined and applied consistently, generally by analogy to Topic 606. The accounting treatment pursuant to Topic 606 is outlined below.

The terms of license, option and collaboration agreements entered into typically include payment of one or more of the following: non-refundable, up-front license fees; option exercise fees; development, regulatory and commercial milestone payments; payments for manufacturing supply and research and development services and royalties on net sales of licensed products. Each of these payments results in license, collaboration and other revenue, except for revenues from royalties on net sales of licensed products, which are classified as royalty revenue. The core principle of Topic 606 is to recognize revenue when promised goods or services are transferred to customers in an amount that reflects the consideration that is expected to be received in exchange for those goods or services. The Company may also receive reimbursement or make payments to a collaboration partner to satisfy cost sharing requirements. These payments are accounted for pursuant to ASC 808 and are recorded as an offset or increase to research and development expenses, respectively.

In determining the appropriate amount of revenue to be recognized as the Company fulfills its obligations under each of its agreements, the Company performs the following steps: (i) identification of the promised goods or services in the contract; (ii) determination of whether the promised goods or services are performance obligations including whether they are distinct in the context of the contract; (iii) measurement of the transaction price, including the constraint on variable consideration; (iv) allocation of the transaction price to the performance obligations based on estimated selling prices; and (v) recognition of revenue when (or as) the Company satisfies each performance obligation.

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Amounts received prior to satisfying the revenue recognition criteria are recorded as contract liabilities in the Company's Condensed Consolidated Balance Sheets. If the related performance obligation is expected to be satisfied within the next twelve months this will be classified in current liabilities. Amounts recognized as revenue prior to the Company having an unconditional right (other than a right that is conditioned only on the passage of time) to receipt are recorded as contract assets in the Company's Condensed Consolidated Balance Sheets. If the Company expects to have an unconditional right to receive the consideration in the next twelve months, this will be classified in current assets. A net contract asset or liability is presented for each contract with a customer.

At contract inception, the Company assesses the goods or services promised in a contract with a customer and identifies those distinct goods and services that represent a performance obligation. A promised good or service may not be identified as a performance obligation if it is immaterial in the context of the contract with the customer, if it is not separately identifiable from other promises in the contract (either because it is not capable of being separated or because it is not separable in the context of the contract), or if the promised good or service does not provide the customer with a material right.

The Company considers the terms of the contract to determine the transaction price. The transaction price is the amount of consideration to which the Company expects to be entitled in exchange for transferring promised goods or services to a customer. The consideration promised in a contract with a customer may include fixed amounts, variable amounts, or both. Variable consideration will only be included in the transaction price when it is not considered constrained, which is when it is probable that a significant reversal in the amount of cumulative revenue recognized will not occur.

If it is determined that multiple performance obligations exist, the transaction price is allocated at the inception of the agreement to all identified performance obligations based on the relative standalone selling prices ("SSP"). The relative SSP for each deliverable is estimated using external sourced evidence if it is available. If external sourced evidence is not available, the Company uses its best estimate of the SSP for the deliverable.

Revenue is recognized when, or as, the Company satisfies a performance obligation by transferring a promised good or service to a customer. An asset is transferred when, or as, the customer obtains control of that asset, which for a service is considered to be as the services are received and used. The Company recognizes revenue over time by measuring the progress toward complete satisfaction of the relevant performance obligation using an appropriate input or output method based on the nature of the service promised to the customer.

After contract inception, the transaction price is reassessed at every period end and updated for changes such as resolution of uncertain events. Any change in the transaction price is allocated to the performance obligations on the same basis as at contract inception, or to a single performance obligation as applicable. The Company accounts for the exercise of a material right as either a contract modification or as a continuation of the existing contract, as is most appropriate based on the facts and circumstances.

Management may be required to exercise considerable judgment in estimating revenue to be recognized. Judgment is required in identifying performance obligations, estimating the transaction price, estimating the SSP of identified performance obligations, which may include forecasted revenue, development timelines, reimbursement rates for personnel costs, discount rates and probabilities of technical and regulatory success, and estimating the progress towards satisfaction of performance obligations.

Comprehensive Loss

Comprehensive loss is composed of net loss and certain changes in stockholders' equity that are excluded from net loss, primarily unrealized gains or losses on the Company's marketable securities.

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Net Loss per Per Share

Basic net loss per share is calculated by dividing the net loss by the weighted-average number of shares of common stock outstanding during the period, without consideration for common stock equivalents. Diluted net loss per share is the same as basic net loss per share, since the effects of potentially dilutive securities are antidilutive given the net loss for each period presented. The weighted-average common shares outstanding as of March 31, 2024 includes pre-funded warrants to purchase shares of common stock that were issued in connection with the February 2024 private placement, as discussed further below in Note 7 - "*Common Stock*".

Recently Issued Accounting Pronouncements

In November 2023, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update No. 2023-07, *Segment Reporting (Topic 280): Improvements to Reportable Segment Disclosures*, which is intended to improve reportable segment disclosure requirements primarily through enhanced disclosures about significant segment expenses. The amendments in this Update are effective for all public entities for fiscal years beginning after December 15, 2023, and interim periods within fiscal years beginning after December 15, 2024, with early adoption permitted. The guidance is to be applied retrospectively to all prior periods presented in the financial statements. The Company is currently evaluating the impact of the new standard on its consolidated financial statements and related disclosures.

In December 2023, the FASB issued Accounting Standards Update No. 2023-09, *Income Taxes (Topic 740): Improvements to Income Tax Disclosures*, which requires that an entity, on an annual basis, disclose additional income tax information, primarily related to the rate reconciliation and income taxes paid. The amendments in this Update are effective to be applied prospectively for annual periods beginning after December 15, 2024, with early adoption permitted. The Company is currently evaluating the impact of the new standard on its income tax disclosures.

2. Fair Value Measurements

Assets and liabilities measured at fair value at each balance sheet date are as follows (in thousands):

	September 30, 2023			
	Level 1	Level 2	Level 3	Total
Assets:				
Cash equivalents:				
Money market funds	$ 93,890	$ —	$ —	$ 93,890
Short-term marketable securities:				
U.S. government treasuries	924,811	—	—	924,811
U.S. government agency securities	—	20,941	—	20,941
Commercial paper	—	15,493	—	15,493
Long-term marketable securities:				
U.S. government treasuries	7,905	—	—	7,905

	March 31, 2024			
	Level 1	Level 2	Level 3	Total
Assets:				
Cash equivalents:				
Money market funds				
Short-term marketable securities:				
U.S. government treasuries				
Corporate debt securities				
Commercial paper				
Long-term marketable securities:				
U.S. government treasuries				

	U.S. government treasuries				
	U.S. government treasuries				
	Corporate debt securities				
	Corporate debt securities				
	Corporate debt securities				
Total	Total	$1,026,606	$36,434	$ —	$1,063,040

	December 31, 2022			
	Level 1	Level 2	Level 3	Total
Assets:				
Cash equivalents:				
Money market funds	$ 105,340	$ —	$ —	$ 105,340
U.S. government treasuries	43,781	—	—	43,781
Commercial paper	—	9,948	—	9,948
Short-term marketable securities:				
U.S. government treasuries	1,003,504	—	—	1,003,504
U.S. government agency securities	—	16,861	—	16,861
Corporate debt securities	—	54,215	—	54,215
Commercial paper	—	43,591	—	43,591
Total	$ 1,152,625	$ 124,615	$ —	$ 1,277,240

The carrying amounts of prepaid expenses and other current assets, accounts payable, accrued liabilities and cost sharing payments due to related party approximate their fair values due to their short-term maturities.

	December 31, 2023			
	Level 1	Level 2	Level 3	Total
Assets:				
Cash equivalents:				
Money market funds	$ 121,034	$ —	$ —	$ 121,034
Short-term marketable securities:				
U.S. government treasuries	869,172	—	—	869,172
U.S. government agency securities	—	7,086	—	7,086
Commercial paper	—	31,147	—	31,147
Total	$ 990,206	$ 38,233	$ —	$ 1,028,439

The Company's Level 2 securities are valued using third-party pricing sources. The pricing services utilize industry standard valuation models, including both income and market-based approaches, for which all significant inputs are observable, either directly or indirectly.

The Company has not transferred any assets or liabilities between the fair value measurement levels. levels for the three months ended March 31, 2024 or 2023.

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3. Marketable Securities

All marketable securities were considered available-for-sale at September 30, 2023 March 31, 2024 and December 31, 2022 December 31, 2023. On a recurring basis, the Company records its marketable securities at fair value using Level 1 or Level 2 inputs as discussed in Note 2, "Fair Value Measurements". The amortized cost, gross unrealized holding gains or losses, and fair value of the Company's marketable securities by major security type at each balance sheet date are summarized in the tables below (in thousands):

		September 30, 2023			
		Amortized Cost	Unrealized Holding Gains	Unrealized Holding Losses	Aggregate Fair Value
		March 31, 2024			March 31, 2024
	Amortized Cost				Amortized Cost	Unrealized Holding Gains	Unrealized Holding Losses	Aggregate Fair Value
Short-term marketable securities:	Short-term marketable securities:							

U.S. government treasuries[1]	U.S. government treasuries[1]	$ 925,091	$ 20	$ (300)	$ 924,811
U.S. government agency securities[2]		20,952	1	(12)	20,941
U.S. government treasuries[1]					
U.S. government treasuries[1]					
Corporate debt securities					
Corporate debt securities					
Corporate debt securities					
Commercial paper	Commercial paper	15,493	—	—	15,493
Total short-term marketable securities	Total short-term marketable securities	961,536	21	(312)	961,245
Long-term marketable securities:	Long-term marketable securities:				
U.S. government treasuries[3]		7,914	—	(9)	7,905
U.S. government treasuries[2]					
U.S. government treasuries[2]					
U.S. government treasuries[2]					
Corporate debt securities[3]					
Corporate debt securities[3]					
Corporate debt securities[3]					
Total long-term marketable securities	Total long-term marketable securities	7,914	—	(9)	7,905
Total	Total	$ 969,450	$ 21	$ (321)	$ 969,150

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(1) Unrealized holding losses on 39 23 securities with an aggregate fair value of $686.2 million $572.9 million.

(2) Unrealized holding losses on 14 securities with an aggregate fair value of $475.2 million.

(3) Unrealized holding losses on 4 securities with an aggregate fair value of $17.5 million.

(3) Unrealized holding loss on 1 security with an aggregate fair value of $7.9 million $15.5 million.

	December 31, 2023			
	Amortized Cost			
Short-term marketable securities:				
U.S. government treasuries				
U.S. government treasuries				
U.S. government treasuries				
U.S. government agency securities[1]				

	December 31, 2023			
	Amortized Cost	Unrealized Holding Gains	Unrealized Holding Losses	Aggregate Fair Value

	December 31, 2022			
	Amortized Cost	Unrealized Holding Gains	Unrealized Holding Losses	Aggregate Fair Value
Short-term marketable securities:				
U.S. government treasuries[1]	$1,009,733	$ 58	$ (6,287)	$1,003,504
U.S. government agency securities	16,823	38	—	16,861
Corporate debt securities[2]	54,571	—	(356)	54,215
Commercial paper				
Commercial paper				
Commercial paper	43,591	—	—	43,591
Total	$1,124,718	$ 96	$ (6,643)	$1,118,171

Total	
Total	

(1) Unrealized holding losses on 51 2 securities with an aggregate fair value of $683.4 million.

(2) Unrealized holding losses on 16 securities with an aggregate fair value of $54.2 million $7.1 million.

As of September 30, 2023 March 31, 2024 and December 31, 2022 December 31, 2023, a majority some of the Company's marketable securities were in an unrealized loss position. The Company has not recognized an allowance for credit losses as of September 30, 2023 March 31, 2024 or December 31, 2022 December 31, 2023. The Company determined that it had the ability and intent to hold all marketable securities that have been in a continuous loss position until maturity or recovery. Further, a majority of these marketable securities are held in U.S. government securities, and the remainder were initially, and continue to be, held with investment grade, high credit quality institutions. All marketable securities with unrealized losses as of each balance sheet date have been in a loss position for less than twelve months or the loss is not material.

As of September 30, 2023 March 31, 2024, all of the Company's marketable securities have an effective maturity of less than two years.

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4. Acquisition and Research Funding Collaboration Agreement

Acquisition of F-star Gamma

In August 2016, the Company entered into a License and Collaboration Agreement ("F-star Collaboration Agreement") with F-star Gamma Limited ("F-star Gamma"), F-star Biotechnologische Forschungs-und Entwicklungsges M.B.H ("F-star GmbH") and F-star Biotechnology Limited ("F-star Ltd") (collectively, "F-star") to leverage F-star's modular antibody technology and the Company's expertise in the development of therapies for neurodegenerative diseases. In May 2018, the Company exercised the pre-negotiated option agreement (the "Option Agreement") under the F-star Collaboration Agreement and entered into a Share Purchase Agreement (the "Purchase Agreement") with the shareholders of F-star Gamma and Shareholder Representative Services LLC, pursuant to which the Company acquired all of the outstanding shares of F-star Gamma (the "Acquisition"). The details of the Acquisition are further described in Note 4, "Acquisition", to the consolidated financial statements in the Company's 2022 2023 Annual Report on Form 10-K.

As of September 30, 2023 March 31, 2024, the Company had paid consideration of $49.8 million in the aggregate consisting of up-front, preclinical, and clinical contingent consideration. The aggregate $49.8 million consideration, payment all of which was recorded as research and development expense as incurred. This amount includes a $30.0 million contingent consideration payment which was triggered and recorded as research and development expense in March 2023 upon the achievement of a specified clinical milestone in the ETV:IDS program, all of which was recognized as research and development expense in the Condensed Consolidated Statements of Operations and Comprehensive Loss in the first quarter of 2023. program. This contingent consideration payment fully satisfies the Company's clinical contingent consideration obligations under the Purchase Agreement. There was no contingent consideration expense recognized for the three months ended September 30, 2023 or March 31, 2024.

Collaboration and Development Funding Agreement

On January 29, 2024, the Company entered into a Collaboration and Development Funding Agreement with an unrelated third party, pursuant to which this third party will provide up to $75.0 million of funding and collaborate with the Company to conduct a global Phase 2a study of BIIB122/DNL151 in patients with Parkinson's disease and confirmed pathogenic variants of LRRK2.

Pursuant to this agreement, an upfront payment of $12.5 million was received in January 2024, with the remainder to be paid based on time and operational milestones in the study. After the full $75.0 million in consideration has been paid, the third party will be eligible to receive low single-digit royalties from the Company on annual worldwide net sales of LRRK2 inhibitors for the treatment of Parkinson's disease.

The Company determined that this arrangement is an R&D funding arrangement under ASC 730. As the third party is sharing in the risk associated with research and development activities with the Company, the development funding is recognized as an obligation to perform contractual services. Accordingly, payments received will be recorded as a liability, and recognized by the Company as a reduction to Research and development expenses over the estimated Phase 2a study period as the underlying research and development costs are incurred. No reduction to research and development expenses was recorded within in the Condensed Consolidated Statements of Operations and Comprehensive Loss for the three and nine months ended September 30, 2022 March 31, 2024. As of March 31, 2024, a liability of $12.5 million was recorded within deferred research funding liability, current on the Condensed Consolidated Balance Sheet.

5. Collaboration Agreements

Biogen

In August October 2020, the Company entered into a binding Provisional Definitive Collaboration and License Agreement ("Provisional LRRK2 Agreement"), pursuant to which it granted Biogen a license toco-develop and co-commercialize its small molecule LRRK2 inhibitor program (the "LRRK2 Program"), and a Right of First Negotiation, Option and License Agreement (the "ROFN and Option Agreement"), pursuant to which it granted an option and right of first negotiation to certain of the Company's programs utilizing our TV technology platform, including its amyloid beta program (collectively the "Biogen Collaboration Agreement" Agreement"), with Biogen Inc.'s subsidiaries, Biogen MA Inc. ("BIMA")

and Biogen International GmbH (“BIG”) (BIMA and BIG, collectively, “Biogen”), which expired in October 2020 upon the execution of a Definitive LRRK2 Collaboration and License Agreement (“LRRK2 Agreement”) with Biogen on October 4, 2020 and a Right of First Negotiation, Option and License Agreement (the “ROFN and Option Agreement”) on October 6, 2020 (collectively, the "Biogen Collaboration Agreement"). The details of the Provisional Biogen Collaboration Agreement and the Biogen Collaboration Agreement and the payments the Company has received, and is entitled to receive, are further described in Note 5, "Collaboration Agreements", to the consolidated financial statements in the 2022 2023 Annual Report on Form 10-K. In August 2023, the Company and Biogen executed an Amendment (the “Biogen Amendment”) to the LRRK2 Agreement and ROFN and Option Biogen Collaboration Agreement. Pursuant to the Biogen Amendment, the schedule of potential LRRK2 Agreement milestones was amended, while maintaining the same total value of milestones that Denali is eligible to receive. In addition, under the Biogen Amendment, Biogen waived its option right to the second option program and waived its rights of first negotiation for two other TV-enabled programs under the ROFN and Option Agreement.The Company has no remaining performance obligations under the Biogen Collaboration Agreement, and therefore no contract liability remained on the Condensed Consolidated Balance Sheets as of March 31, 2024 or December 31, 2023.

During

There were no changes to the nine terms of the Biogen Collaboration Agreement during the three months ended September 30, 2023 March 31, 2024 or 2023. As of December 31, 2023, Biogen exercised its option to license Denali’s ATV:Abeta program which was previously concluded to be no longer considered a material right. Biogen provided additional consideration of $5.0 million at the time of exercise which was fully allocated to the material right. The option exercise was accounted for as a continuation of the existing contract, and resulted in the delivery of the ATV:Abeta Program License. The $288.9 million related party contract liability associated with the material right as defined in ASC 850.

The Company recorded $4.8 million and $4.2 million of cost sharing payments to Biogen for the ATV:Abeta option, LRRK2 development activities in research and the $5.0 million option fee were both allocated to this performance obligation which was satisfied upon transfer of the ATV:Abeta Program License in April 2023. Accordingly, related-party collaboration revenue from customers of $293.9 million was recognized development expenses in the Condensed Consolidated Statements of Operations and Comprehensive Loss during the nine months ended September 30, 2023. No change in the transaction price for the Biogen Collaboration Agreement was recorded during the three months ended September 30, 2023 and three and nine months ended September 30, 2022.

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As a result of the Biogen Amendment, the related-party contract liability of $1.3 million related to the Option Research Services for the second option program, the only remaining performance obligation under the Biogen Collaboration Agreement, was considered fully satisfied, and as such this contract liability was recognized in full within collaboration revenue from customers during the three months ended September 30, 2023. No related-party contract liability remains on the Condensed Consolidated Balance Sheet as of September 30, 2023. A related-party contract liability of $290.5 million was recorded on the Consolidated Balance Sheet as of December 31, 2022.

The Company recorded incremental research and development expenses in the Condensed Consolidated Statement of Operations and Comprehensive Loss of $3.4 million and $1.4 million for the three months ended September 30, 2023 March 31, 2024 and 2022, respectively, and $14.5 million and $3.8 million for the nine months ended September 30, 2023 and 2022, respectively, representing cost sharing payments owed to Biogen for LRRK2 development activities. Cost 2023, respectively. Cost sharing payments due to related party Biogen of $10.4 $4.8 million and $3.2 million and $4.4 million were recorded within accounts payable on the Condensed Consolidated Balance Sheets as of September 30, 2023 March 31, 2024 and December 31, 2022 December 31, 2023, respectively.

As of September 30, 2023 March 31, 2024, the Company had earned $5.0 million in option fee payments, but has had not recorded milestone revenue or product sales under the Biogen Collaboration Agreement.

Sanofi

In October 2018, the Company entered into a Collaboration and License Agreement ("Sanofi Collaboration Agreement") with Genzyme Corporation, a wholly owned subsidiary of Sanofi S.A. ("Sanofi"). The details of the Sanofi Collaboration Agreement and the payments the Company has received, and is entitled to receive, are further described in Note 5, "Collaboration Agreements", to the consolidated financial statements in the Company's 2022 2023 Annual Report on Form 10-K. The Company has no remaining performance obligations under the Sanofi Collaboration Agreement, and therefore no contract liability remains on the Condensed Consolidated Balance Sheets as of September 30, 2023 March 31, 2024 or December 31, 2022 December 31, 2023.

During the three and nine months ended September 30, 2023, there There were no changes to the terms of the Sanofi Collaboration Agreement. There was no revenue or changes in transaction price for Agreement during the three months ended September 30, 2023 March 31, 2024 or 2022. The transaction price increased by $25.0 million and $40.0 million for the nine months ended September 30, 2023 and 2022, respectively, related to clinical milestones received, which were recognized in full within collaboration revenue from customers in the Condensed Consolidated Statements of Operations and Comprehensive Loss in the period in which they were earned.

2023. As of September 30, 2023 March 31, 2024, the Company had earned milestone payments of $100.0 million and had not recorded any product sales under the Sanofi Collaboration Agreement.

Takeda

PTV:PGRN and ATV:TREM2 Collaboration Agreements

In January 2018, the Company entered into a Collaboration and Option Agreement ("Takeda Collaboration Agreement") with Takeda Pharmaceutical Company Limited ("Takeda"). The details of the Takeda Collaboration Agreement are further described in Note 5, "Collaboration Agreements", to the consolidated financial statements in the Company's 2022 2023 Annual Report on Form 10-K. There are no remaining performance obligations or potential payments remaining under the initial Takeda Collaboration Agreement.

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The opt-in by Takeda on the PTV:PGRN and ATV:TREM2 programs represented two new contracts with a customer for accounting purposes (the "PTV:PGRN Collaboration Agreement" and the "ATV:TREM2 Collaboration Agreement"), both of which became effective in December 2021. The details of the PTV:PGRN Collaboration Agreement and the ATV:TREM2 Collaboration Agreement are further described in Note 5, "Collaboration Agreements", to the consolidated financial statements in the Company's 2022 2023 Annual Report on Form 10-K.

During the three and nine months ended September 30, 2023, there There were no changes to the terms of the ATV:TREM2 or PTV:PGRN Collaboration Agreements. During Agreements during the three months ended September 30, 2023, and the three and nine months ended September 30, 2022, there were no changes to the transaction prices for either the PTV:PGRN March 31, 2024 or ATV:TREM2 Collaboration Agreements. The transaction price increased by $10.0 million in the nine months ended September 30, 2023 related to a clinical milestone received, which was recognized in full within collaboration revenue from customers in the Condensed Consolidated Statements of Operations and Comprehensive Loss in the period in which it was earned.2023.

The Company recorded $1.7 million $1.2 million and $5.1 million $1.5 million of cost sharing reimbursements for PTV:PGRN development activities, and $1.1 million $0.5 million and $4.3 million $1.7 million for ATV:TREM2 development activities, for the three and nine months ended September 30, 2023, respectively, as offsets to research March 31, 2024 and development expenses in the Condensed Consolidated Statements of Operations and Comprehensive Loss. The Company recorded $2.3 million and $8.0 million of cost sharing reimbursements for PTV:PGRN development activities, and $1.6 million and $5.2 million for ATV:TREM2 development activities, for the three and nine months ended September 30, 2022, 2023, respectively, as offsets to research and development expenses in the Condensed Consolidated Statements of Operations and Comprehensive Loss. Cost sharing reimbursements of $2.1 $1.9 million and $8.9 $2.7 million were recorded as receivables a receivable within prepaid expenses and other current assets on the Condensed Consolidated Balance Sheets as of September 30, 2023 March 31, 2024 and December 31, 2022 December 31, 2023, respectively.

As of September 30, 2023 March 31, 2024, the Company had earned an aggregate of $10.0 million in option fee payments and $10.0 million in milestone payments from Takeda under the PTV:PGRN and ATV:TREM2 Collaboration Agreements, and had not recorded any product sales under either agreement.

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Collaboration Revenue

Revenue disaggregated by collaboration agreement and performance obligation is as follows (in thousands):

	Three Months Ended March 31,	Three Months Ended March 31,	Three Months Ended March 31,
	2024	2024	2024
Takeda Collaboration Agreement:			
Takeda Collaboration Agreement:			
Takeda Collaboration Agreement:			
PTV:PGRN Collaboration Agreement(1)			
PTV:PGRN Collaboration Agreement(1)			
PTV:PGRN Collaboration Agreement(1)			
Total Takeda Collaboration Revenue			
Total Takeda Collaboration Revenue			
Total Takeda Collaboration Revenue			
Sanofi Collaboration Agreement			
Sanofi Collaboration Agreement			
Sanofi Collaboration Agreement			
CNS Program License(2)			
CNS Program License(2)			
CNS Program License(2)			

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2023	2022	2023	2022
Takeda Collaboration Agreement:				
Takeda Collaboration Agreement Services[1]	$ —	$ —	$ —	$ 51,916
PTV:PGRN Collaboration Agreement	—	—	10,000	—
Total Sanofi Collaboration Revenue				
Total Takeda Collaboration Revenue	—	—	10,000	51,916
Sanofi Collaboration Agreement				
CNS Program License	—	—	25,000	40,000
Alzheimer's Disease Services[2]	—	3,375	—	3,375
Total Sanofi Collaboration Revenue				
Total Sanofi Collaboration Revenue	—	3,375	25,000	43,375
Biogen Collaboration Agreement				
Biogen Collaboration Agreement				
ATV:Abeta Program License[3]	—	—	293,912	—
Option Research Services[2]	1,267	184	1,619	2,889
Option Research Services[3]				
Option Research Services[3]				
Option Research Services[3]				
Total Biogen Collaboration Revenue				
Total Biogen Collaboration Revenue	1,267	184	295,531	2,889
Total Collaboration Revenue	$ 1,267	$ 3,559	$ 330,531	$ 98,180
Total Collaboration Revenue				

(1) Revenue of $27.9 million for the nine three months ended September 30, 2022 March 31, 2023 from a specified clinical milestone in the Phase 1/2 clinical of DNL593 in patients with frontotemporal dementia-granulin (FTD-GRN).

(2) Revenue for the three months ended March 31, 2023 from a milestone payment triggered and received in January 2023 upon the commencement of dosing in a Phase 2 study of SAR443820/DNL788 in individuals with multiple sclerosis.

(3) Revenue for the three months ended March 31, 2023 was included in the contract liability balance at the beginning of the period.

(2) Revenue for all periods presented was included in the contract liability balance at the beginning of the respective period.

(3) Revenue of $288.9 million for nine months ended September 30, 2023 was included in the related-party contract liability balance at the beginning of the period.

6. License Agreement

Genentech

In June 2016, the Company entered into an Exclusive License Agreement with Genentech, Inc. (“Genentech License Agreement”). The details of the Genentech License Agreement are further described in Note 6, "License Agreements", to the consolidated financial statements in the Company's 2022 Annual Report on Form 10-K. No expenses were recorded under the Genentech License Agreement for the three and nine months ended September 30, 2023. In the nine months ended September 30, 2022, the Company paid Genentech two clinical milestone payments of $7.5 million and $5.0 million, triggered upon the commencement of dosing in the global Phase 2b LUMA study to evaluate the efficacy and safety of BIIB122/DNL151, and the commencement of dosing in the global Phase 3 LIGHTHOUSE study to evaluate the efficacy and safety profile of BIIB122/DNL151, respectively, by the Company's collaboration partner Biogen. Biogen is responsible for 50% of any payment obligation to Genentech under the Biogen Collaboration Agreement, including these clinical milestones, and accordingly $2.5 million and $6.3 million of research and development expense was recorded in the three and nine months ended September 30, 2022, respectively, in the Condensed Consolidated Statements of Operations and Comprehensive Loss.

To date, the Company has made payments to Genentech of $25.0 million in the aggregate, including an upfront fee, a technology transfer fee and three clinical milestone payments, with $18.8 million of the payments recorded as research and development expense as incurred, net of cost sharing reimbursements from Biogen.

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7. Commitments and Contingencies

Lease Obligations

In May 2018, the Company entered into an operating lease for its corporate headquarters in South San Francisco (the "Headquarters Lease"), as further described in Note 8, "Commitments and Contingencies," to the consolidated financial statements in the Company's 2022 2023 Annual Report on Form 10-K. In August 2021, the Company entered into an operating lease for laboratory, office and warehouse premises in Salt Lake City, Utah (the "SLC Lease"). In March 2023, the Company terminated the SLC Lease, which resulted in the recognition of $7.9 million of accelerated depreciation on leasehold improvements in the nine three months ended September 30, March 31, 2023. The SLC Lease had not commenced for accounting purposes, and as such, no lease liability or ROU asset was recorded on the Condensed Consolidated Balance Sheet, and no operating lease expense was recorded associated with this lease.

In April 2023, the Company entered into a new operating lease in Salt Lake City for a 59,336 square foot laboratory, office and warehouse premises with a contractual term of approximately 15.0 15 years upon commencement, and future undiscounted lease payments of approximately $13.4 million. , which was subsequently amended in October 2023. For accounting purposes, this new lease has not yet commenced, and as such, no lease liability or ROU asset is recorded on the Condensed Consolidated Balance Sheet Sheets as of September 30, 2023 March 31, 2024 and December 31, 2023, and no operating lease expense has been recorded on the Condensed Consolidated Statements of Operations and Comprehensive Loss for the three and nine months ended September 30, 2023 March 31, 2024.

Management exercised judgment in applying the requirements of ASC 842, including the determination as to whether certain contracts contain a lease, the lease consideration, and the commencement date of the lease, and for leases identified under the standard, the discount rate used to determine the measurement of the lease liability. The discount rates of our operating leases are an approximation of the Company's incremental borrowing rate and are dependent upon the term and economics of the agreement. To estimate the incremental borrowing rate, management considers observable debt yields of comparable market instruments, as well as benchmarks within the lease agreement that may be indicative of the rate implicit in the lease. There were no changes to the terms of the leases recognized under ASC 842 during the three or nine months ended September 30, 2023 March 31, 2024.

Operating lease costs, including variable costs recognized under ASC 842, were $3.2 million and $9.4 million was $2.9 million for both the three and nine months ended September 30, 2023, respectively, March 31, 2024 and $3.3 million and $8.7 million for the three and nine months ended September 30, 2022, respectively. 2023. The following table contains a summary of other information pertaining to the Company's operating lease for the periods presented (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2023	2022	2023	2022
Cash paid for amounts included in measurement of lease liabilities	$2,793	$2,899	$8,552	$8,193

	Three Months Ended March 31,	
	2024	2023
Cash paid for amounts included in measurement of lease liabilities		

	As of September 30,	
	2023	2022
Weighted average remaining lease term	5.6 years	6.4 years

	As of March 31,	
	2024	2023
Weighted average remaining lease term	5.1 years	6.1 years

Weighted average discount rate	Weighted average discount rate	9.0%	8.9%	Weighted average discount rate	9.0	%	9.0	%

The following table reconciles the undiscounted cash flows for the next five years and total of the remaining years to the operating lease liabilities recorded in the Condensed Consolidated Balance Sheet as of September 30, 2023 March 31, 2024 (in thousands):

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Year Ended December 31:	Year Ended December 31:		
2023 (three months)			2,793
2024			11,417
2024 (nine months)			
2024 (nine months)			
2024 (nine months)			
2025	2025		11,793
2026	2026		12,182
2027	2027		12,584
2028			
Thereafter	Thereafter		17,381
Total undiscounted lease payments	Total undiscounted lease payments		68,150
Present value adjustment	Present value adjustment		(14,249)
Net operating lease liabilities		$	53,901
Net operating lease liability			

Indemnification

In the ordinary course of business, the Company may provide indemnifications of varying scope and terms to vendors, lessors, business partners, board members, officers, and other parties with respect to certain matters, including, but not limited to, losses arising out of breach of such agreements, services to be provided by the Company, negligence or willful misconduct of the Company, violations of law by the Company, or from intellectual property infringement claims made by third parties. In addition, the Company has entered into indemnification agreements with directors and certain officers and employees that will require the Company, among other things, to indemnify them against certain liabilities that may arise by reason of their status or service as directors, officers or employees. No demands have been made upon the Company to provide indemnification under such agreements, and thus, there are no claims that the Company is aware of that could have a material effect on the Company's Condensed Consolidated Balance Sheets, Condensed Consolidated Statements of Operations and Comprehensive Loss, or Condensed Consolidated Statements of Cash Flows. Flows.

Commitments

Effective September 2017, the Company entered into a Development and Manufacturing Services Agreement as amended ("DMSA") with Lonza Sales AG ("Lonza") for the development and manufacture of biologic products. Under the DMSA, the Company will execute purchase orders based on project plans authorizing Lonza to provide development and manufacturing services with respect to certain of the Company's antibody and enzyme products, and will pay for the services provided and batches delivered in accordance with the DMSA and project plan. Unless earlier terminated, the DMSA will expire when all development and manufacturing services are completed, which is not expected to be before November 2029. As of September 30, 2023 March 31, 2024 and December 31, 2022 December 31, 2023, the Company had total non-cancellable purchase commitments under the DMSA of $49.9 million $33.1 million and $32.3 million $37.6 million, respectively.

During the three months ended September 30, 2023 March 31, 2024 and 2022, 2023, the Company incurred costs of $10.4 million $16.4 million and $3.4 $5.2 million, respectively, and made payments of $12.8 million $13.5 million and $3.9 million, respectively, for the development and manufacturing services rendered under the DMSA. During the nine months ended September 30, 2023 and 2022, the Company incurred costs of $26.5 million and $22.9 million, respectively, and made payments of $24.9 million and $19.6 million $3.8 million, respectively, for the development and manufacturing services rendered under the DMSA.

In the normal course of business, the Company enters into other firm purchase commitments primarily related to research and development activities. The Company had contractual obligations under certain clinical and manufacturing agreements other than the DMSA of $37.8 million $34.5 million and $9.6 million $34.8 million, as of September 30, 2023 March 31, 2024 and December 31, 2022 December 31, 2023, respectively, with certain amounts subject to cost sharing with Takeda.

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Contingencies

From time to time, the Company may be involved in lawsuits, arbitration, claims, investigations and proceedings consisting of intellectual property, employment and other matters which arise in the ordinary course of business. The Company records accruals for loss contingencies to the extent that the Company concludes that it is probable that a liability has been incurred and the amount of the related loss can be reasonably estimated.

7. Common Stock

On February 27, 2024, the Company entered into a securities purchase agreement (the "Purchase Agreement") with certain investors for the private placement of (i) 3,244,689 shares of Denali's common stock at a price of $17.07 per share and (ii) pre-funded warrants to purchase an aggregate of 26,046,065 shares of Denali's common stock (the "Pre-Funded Warrants") at a purchase price of $17.06 per Pre-Funded Warrant, which represents the per share price for the common stock less the $0.01 exercise price. The private placement closed on February 29, 2024, at which time the Company received aggregate net proceeds of approximately $499.3 million, after deducting issuance costs of approximately $0.5 million.

The Pre-Funded Warrants were classified as a component of permanent equity in the Company's consolidated balance sheet as they are freestanding financial instruments that are immediately exercisable, do not embody an obligation for the Company to repurchase its shares and permit the holders to receive a fixed number of shares of common stock upon exercise. As of March 31, 2024, all of the Pre-Funded Warrants issued in the private placement were outstanding.

8. Stock-Based Awards

The Company has issued stock-based awards from various equity incentive and stock purchase plans, as more fully described in Note 9, "Stock-Based Awards" to the consolidated financial statements in the Company's 2022 2023 Annual Report on Form 10-K.

Stock Option Activity

The following table summarizes stock option activity for the nine three months ended September 30, 2023 March 31, 2024:

	Number of Options	Weighted-Average Exercise Price
Balance at December 31, 2022	14,673,717	$ 27.03
Granted	3,395,331	27.68
Exercised	(795,686)	12.20
Forfeited	(597,984)	40.37
Balance at September 30, 2023	16,675,378	$ 27.39
Vested and expected to vest at September 30, 2023	15,865,507	$ 29.91
Exercisable at September 30, 2023	10,721,238	$ 25.28

	Number of Options	Weighted-Average Exercise Price
Balance at December 31, 2023	16,490,551	$ 27.34
Granted	4,171,102	20.33
Exercised	(130,214)	7.85
Forfeited	(804,563)	28.50
Balance at March 31, 2024	19,726,876	$ 25.94
Vested and expected to vest at March 31, 2024	18,917,005	$ 27.02
Exercisable at March 31, 2024	11,826,599	$ 26.70

The estimated fair value of stock options granted to employees were calculated using the Black-Scholes option-pricing model using the following assumptions:

	Nine Months Ended September 30,

	2023	2022
	Three Months Ended March 31,	
	2024	
Expected term (in years)	Expected term (in years)	5.50 - 6.08	5.50 - 6.08
Volatility	Volatility	67.9% - 69.6%	65.1% - 66.1%
Risk-free interest rate	Risk-free interest rate	3.4% - 4.3%	1.5% - 3.3%
Dividend yield	Dividend yield	—	—

	Three Months Ended March 31,	
	2024	2023
Expected term (in years)	6.08	6.08
Volatility	64.5% - 64.6%	69.1% - 69.6%
Risk-free interest rate	3.9% - 4.0%	3.6% - 4.2%
Dividend yield	—	—

Restricted Stock Activity

The following table summarizes restricted stock unit ("RSU") activity for the nine three months ended September 30, 2023 March 31, 2024:

	Number of RSU shares	Weighted-Average Fair Value at Date of Grant per Share
Unvested at December 31, 2022	3,330,654	$ 41.39
Granted	1,811,640	27.54
Vested and released	(1,132,305)	38.55
Forfeited	(293,478)	36.69
Unvested and expected to vest at September 30, 2023	3,716,511	$ 35.87

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	Number of RSU shares	Weighted-Average Fair Value at Date of Grant per Share
Unvested at December 31, 2023	3,635,157	$ 35.60
Granted	1,919,193	20.23
Vested and released	(752,455)	39.78
Forfeited	(504,807)	28.86
Unvested and expected to vest at March 31, 2024	4,297,088	$ 28.79

Stock-Based Compensation Expense

The Company's results of operations include expenses relating to stock-based compensation as follows (in thousands):

		Three Months Ended September 30,		Nine Months Ended September 30,	
		2023	2022	2023	2022
		Three Months Ended March 31,			
		Three Months Ended March 31,			
		Three Months Ended March 31,			
		2024			
		2024			
		2024			
Research and development					
Research and development					
Research and development	Research and development	$ 15,821	$ 14,716	$ 47,795	$ 45,144
General and administrative	General and administrative	11,638	9,863	34,319	29,516
General and administrative					
General and administrative					
Total	Total	$ 27,459	$ 24,579	$ 82,114	$ 74,660
Total					
Total					

9. Net Loss Per Share

Since the Company was in a loss position for all periods presented, basic net loss per share is the same as diluted net loss per share for all periods as the inclusion of all potential shares of common stock outstanding would have been anti-dilutive. The following table sets forth the computation of basic and diluted net loss per share (in thousands, except share and per share amounts):

	Three Months Ended March 31,	
	2024	2023
Numerator:		
Net loss	$ (101,802)	$ (109,781)
Denominator:		
Weighted average number of:		
Common stock shares outstanding	140,245,132	136,524,528
Private placement pre-funded warrants	9,159,056	—
Total	149,404,188	136,524,528
Net loss per share	$ (0.68)	$ (0.80)

Potentially dilutive securities, including all options issued and outstanding, ESPP shares issuable, and restricted shares subject to future vesting that were not included in the diluted per share calculations for all periods presented because they would be anti-dilutive totaled approximately 20.7 million 24.4 million and 18.4 million 21.4 million shares as of September 30, 2023 March 31, 2024 and September 30, 2022 March 31, 2023, respectively.

10. Divestiture of Preclinical Small Molecule Programs

On March 1, 2024, the Company divested certain assets, including specified intellectual property, tangible assets, and equipment used to conduct early stage small molecule drug discovery ("Divested Assets") through an Asset Purchase and License Agreement (the "Asset Purchase Agreement") executed with a venture-backed private company ("VBPC"). Additionally, certain of the Company's employees terminated their employment with the Company and became employees of VBPC.

Table In exchange for the Divested Assets, the Company received equity consideration in the form of Contentsa simple agreement for future equity ("SAFE"), equal to $15.0 million of equity in VBPC's next financing round or, if VBPC's next equity financing does not occur prior to December 31, 2024, a number of shares of preferred stock issued in VBPC's previous round of equity financing prior to this agreement equal to $15.0 million divided by the price per share paid by investors in that previous equity financing. The Company may also be eligible to receive certain win state, development and sales based milestone payments up to approximately $1.2 billion in the form of either cash or equity at the election of VBPC. The Company will also be entitled to receive future royalties on aggregate net sales of any products that bind to certain identified targets, on a product-by-product and country-by-country basis during the periods of time commencing at the time of the first commercial sale of such product in such country, until the later of (i) the expiration of certain related patents, (ii) the expiration of Regulatory Exclusivity, or (iii) ten years after such first commercial sale.

Concurrently, VBPC and the Company also entered into a sublease for 12,985 square feet of office and lab space within the Company's corporate headquarters, and transition and research services agreement ("Service Agreements"). The sublease is expected to commence in May 2024 for a period of approximately ten months, with two optional six month extension periods. The Service Agreements allow Denali to provide access to equipment and provision of certain specified administrative and research services to VBPC for a period up to the end of the sublease term.

This divestiture did not meet the criteria for reporting discontinued operations as the sale does not represent a strategic shift in the Company's business. The Company recognized a gain on divestiture of approximately $14.5 million in the Condensed Consolidated Statements of Operations and Comprehensive Loss during the three months ended March 31, 2024, representing the difference between the fair value of the consideration received and the carrying amount of the Divested Assets.

The Company recorded the SAFE at $15.0 million based on the expected value of the equity to be received within other non-current assets in the Condensed Consolidated Balance Sheet as of March 31, 2024.

ITEM 2. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

The following discussion and analysis of our financial condition and results of operations should be read together with our condensed consolidated financial statements and the related notes to those statements included elsewhere in this Quarterly Report on Form 10-Q. This discussion and analysis and other parts of this report contain forward-looking statements based upon current beliefs, plans, and expectations related to future events and our future financial performance that involve risks, uncertainties, and assumptions, such as statements regarding our intentions, plans, objectives, expectations, forecasts, and projections. Our actual results and the timing of selected events could differ materially from

those anticipated in these forward-looking statements as a result of several factors, including those set forth under the section titled "Risk Factors" included in this Quarterly Report on Form 10-Q.

Forward-looking statements include, but are not limited to, statements about:

- *the progress, success, cost, and timing of our development activities, preclinical studies, and clinical trials, and in particular the development of our blood-brain barrier ("BBB") platform technology, programs, and biomarkers, including the initiation and completion of studies or trials and related preparatory work, enrollment in such trials, the timing of when data from clinical trials will become available, the advancement of new molecule entities into clinical development and related timing, and the filing of investigational new drug applications or clinical trial applications;*
- *the impact of preclinical findings on our ability to achieve exposures of our product candidates that allow us to explore a robust pharmacodynamic range of these candidates in humans;*
- *the expected potential benefits and potential revenue resulting from strategic collaborations with third parties and our ability to attract collaborators with development, regulatory, and commercialization expertise;*
- *the timing or likelihood of regulatory filings and approvals;*
- *our ability to obtain and maintain regulatory approval of our product candidates, and any related restrictions, limitations, and/or warnings in the label of any approved product candidate;*
- *the extent to which any dosing limitations that we have been subject to, and/or may be subject to in the future, may affect the success of our product candidates;*
- *the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates and technology;*
- *the terms and conditions of licenses granted to us and our ability to license and/or acquire additional intellectual property relating to our product candidates and BBB platform technology;*
- *our ability to obtain funding for our operations, including funding necessary to develop and commercialize our current and potential future product candidates;*
- *our plans and ability to establish sales, marketing, and distribution infrastructure to commercialize any product candidates for which we obtain approval;*
- *future agreements with third parties in connection with the commercialization of our product candidates;*
- *the size and growth potential of the markets for our product candidates, if approved for commercial use, and our ability to serve those markets;*

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- *the rate and degree of market acceptance of our product candidates;*
- *existing regulations and regulatory developments in the United States and foreign countries;*
- *potential claims relating to our intellectual property and third-party intellectual property;*
- *our ability to contract with third-party suppliers and manufacturers and their ability to perform adequately;*
- *our plans and ability to develop our own manufacturing facilities;*
- *the pricing and reimbursement of our product candidates, if approved and commercialized;*
- *the success of competing products or platform technologies that are or may become available;*
- *our ability to attract and retain key managerial, scientific, and medical personnel;*
- *the accuracy of our estimates regarding expenses, future revenue, capital requirements, and needs for additional financing;*
- *our ability to enhance operational, financial, and information management systems;*
- *the impact of adverse economic conditions such as instability in the financial services sector, rising interest rates, rising inflation, and increased labor market competition;*
- *the impact of the COVID-19 pandemic, increased geopolitical uncertainty, a pandemic or other global health emergency, and related global economic disruptions and social conditions on our business;*
- *expectations regarding the intended use of proceeds from our February 2024 Private Investment in Public Equity ("PIPE") financing; and*

- *our financial performance.*

These forward-looking statements are subject to a number of risks, uncertainties, and assumptions, including those described in "Risk Factors." In some cases, you can identify these statements by terms such as "anticipate," "believe," "could," "estimate," "expects," "intend," "may," "plan," "potential," "predict," "project," "should," "will," "would," or the negative of those terms, and similar expressions that convey uncertainty of future events or outcomes. These forward-looking statements reflect our beliefs and views with respect to future events and are based on estimates and assumptions as of the date of this Quarterly Report on Form 10-Q and are subject to risks and uncertainties. We discuss many of these risks in greater detail in the section entitled "Risk Factors" included in Part II, Item 1A and elsewhere in this report. Moreover, we operate in a very competitive and rapidly changing environment. New risks emerge from time to time. It is not possible to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. Given these uncertainties, you should not place undue reliance on these forward-looking statements. We qualify all of the forward-looking statements in this Quarterly Report on Form 10-Q by these cautionary statements. Except as required by law, we assume no obligation to update these forward-looking statements publicly, or to update the reasons actual results could differ materially from those anticipated in any forward-looking statements, whether as a result of new information, future events, or otherwise.

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Overview

Our goal is to discover, develop and deliver therapeutics to defeat degeneration.

Our discovery and development strategy is guided by three overarching principles that we believe will significantly increase the probability of success and accelerate the timing to bring effective therapeutics to patients people living with neurodegenerative diseases: and lysosomal storage diseases:

- **Degenogene Pathways Degenogenes: Genetic Pathway Realization**– each of our programs addresses a molecular target or biological pathway that is genetically validated to cause or increase the risk for neurodegenerative diseases.

- **BBB Platform Technology Brain Delivery: Validation and Optionality**– we engineer our product candidates to cross the BBB and act directly in the brain by following a rigorous approach in designing small molecules and by using our brain. Our proprietary TV transport vehicle ("TV") platform technology is designed to effectively deliver large therapeutic molecules, such as enzymes, proteins, antibodies, and oligonucleotides, across the BBB after intravenous administration.

- **Biomarker-Driven Development and Approval**– we discover, develop and use biomarkers to inform dose selection, assess clinical activity, and to identify patients most likely to respond to our therapies. We are actively engaged in discussions with health authorities regarding the potential use of biomarkers as primary clinical endpoints to support faster paths to approval.

Our late and mid-stage clinical-stage large molecule al programs are: are as follows:

- Tividenofusp alfa (DNL310, ETV:IDS), our lead enzyme replacement therapy ("ERT") program enabled by our Enzyme Transport Vehicle ("ETV" ("ETV"). ETV:IDS, is designed to cross the BBB and restore iduronate duronate 2-sulfatase ("IDS"), and reduce glycosaminoglycans ("GAGs"), both peripherally and in the brain, in patients individuals with mucopolysaccharidosis II ("MPS II", or "Hunter syndrome");

- DNL343, our recombinant progranulin eukaryotic initiation factor 2 B ("PGRN" eIF2B") biotherapeutic enabled by activator program to address diseases such as amyotrophic lateral sclerosis ("ALS") and frontotemporal dementia ("FTD");

- BIIB122/DNL151, our Protein Transport Vehicle leucine-rich repeat kinase 2 ("PTV:PGRN" LRRK2"), inhibitor program, being developed in collaboration with Takeda, Biogen, to address certain types of frontotemporal dementia Parkinson's disease ("FTD" PD");

- SAR443820/DNL788, our CNS-penetrant receptor interacting serine/threonine protein kinase 1 ("RIPK1") inhibitor program, being developed in collaboration with Sanofi, to address neurological diseases such as multiple sclerosis ("MS") and Alzheimer's disease; and

- Eclitasertib (SAR443122/DNL758), especially FTD-GRN caused by PGRN deficiency; a peripheral and non-CNS penetrant RIPK1 inhibitor, being developed in collaboration with Sanofi, to address peripheral inflammatory diseases such as ulcerative colitis ("UC").

Our early-stage clinical programs are as follows:

- DNL126 (ETV:SGSH), our second most advanced ETV enabled program, which is designed to restore lysosomal activity of N-sulfoglucosamine sulfohydrolase ("SGSH"), an enzyme responsible for degrading heparan sulfates in the lysosome, in patients individuals with MPS IIIA (Sanfilippo syndrome Type A);

Our clinical-stage small molecule programs are: and

- TAK-594/DNL593 (PTV:PGRN), our leucine-rich repeat kinase 2 recombinant progranulin ("LRRK2" PGRN") inhibitor program, biotherapeutic enabled by our Protein Transport Vehicle ("PTV:PGRN"), being developed in collaboration with Biogen, Takeda, to address Parkinson's disease frontotemporal dementia-granulin ("PD");

- our eukaryotic initiation factor 2 B ("eIF2B" FTD-GRN") activator program to address diseases such as amyotrophic lateral sclerosis ("ALS") and FTD; caused by PGRN deficiency.

- our CNS-penetrant receptor interacting serine/threonine protein kinase 1 ("RIPK1") inhibitor program, partnered with Sanofi, to address neurological diseases such as ALS, multiple sclerosis ("MS") and Alzheimer's disease; and

- a second non-CNS penetrant RIPK1 inhibitor, partnered with Sanofi, to address peripheral inflammatory diseases such as ulcerative colitis ("UC").

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The following table summarizes key information about our clinical stage programs:

Program	Product Candidate	Clinical Study(ies)	Indication	Operational Control
ETV:IDS	tividenofusp alfa, or DNL310	Ph 1/2	Hunter syndrome (MPS II)	Denali
		Ph 2/3		
eIF2B	DNL343	Ph 1b	ALS	Denali
PTV:PGRN		TAK-594/DNL593	Ph 1/2 2/3	ALS
LRRK2	BIIB122/DNL151	Ph 2a (planned) Ph 2b	Parkinson's disease	Denali Joint with Biogen
RIPK1 (CNS-penetrant)	SAR443820/DNL788	Ph 2	MS	Sanofi
RIPK1 (Peripheral)	eclitasertib, or SAR443122/DNL758	Ph 2	UC	Sanofi
ETV:SGSH	DNL126	Ph 1/2 (planned)	Sanfilippo syndrome Type A (MPS IIIA)	Denali
PTV:PGRN	LRRK2 TAK-594/DNL593	BIIB122/DNL151	Ph 2b	Parkinson's disease
eIF2B	DNL343	Ph 1b 1/2 (paused)[1]	FTD-GRN	ALS
		Ph 2/3	ALS	Joint with Healey Center Takeda
	Ph 2	MS	Sanofi	
RIPK1 (Peripheral)	eclitasertib, or SAR443122/DNL758	Ph 2 (closing)	CLE	Sanofi
		Ph 2	UC	Sanofi

(1) Study has been voluntarily paused in order to implement protocol modifications and is expected to resume later this year.

Since we commenced operations, we have devoted substantially all of our resources to discovering, acquiring and developing product candidates, building our BBB platform technology and assembling our core capabilities in understanding key neurodegenerative disease pathways.

Key operational and financing milestones in 2023 2024 to date include:

- In January 2023, our collaboration partner Sanofi commenced dosing in the Phase 2 study of SAR443820/ DNL788 in patients with MS, triggering a $25.0 million milestone payment, which was received in January 2023;

- In February 2023, at the WORLDS*ymposium*™, we reported additional interim data from the open-label, single-arm Phase 1/2 study of DNL310. Over 49 weeks of DNL310 treatment in the Phase 1/2 study, positive changes across measures of exploratory clinical outcomes including VABS-II (adaptive behavior) and BSID-III (cognitive capabilities) scores and global impression scales were observed. The data also suggested that DNL310 improved hearing, as assessed by auditory brainstem response testing. Additional biomarker data out to 49 weeks continued to demonstrate that DNL310 enabled rapid and sustained normalization of cerebrospinal fluid ("CSF") heparan sulfate to normal healthy levels and improvement in lysosomal function biomarkers. Reduction in urine heparan sulfate and dermatan sulfate after switch from standard of care to DNL310 suggested additional sustained peripheral activity of DNL310. The DNL310 safety profile, with up to two years of treatment, remained consistent with standard of care;

- In March 2023, a contingent consideration payment of $30.0 million associated with our acquisition of F-star Gamma was triggered upon the achievement of a specified clinical milestone in the ETV:IDS program. This payment fully satisfies our clinical contingent consideration obligations under the Purchase Agreement;

- In March 2023, a $10.0 million milestone payment from Takeda was triggered upon achievement of a specified clinical milestone in the Phase 1/2 study of TAK-594/DNL593 in patients with FTD-GRN, which we received in May 2023;

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- In April 2023, we entered into a new operating lease in Salt Lake City, Utah for a 59,336 square foot laboratory (the "Utah site"), office and warehouse premises, after terminating our previous SLC lease in March 2023, decreasing future lease payments by $6.1 million while increasing the lease term by approximately five and a half years. The Utah site will expand our clinical manufacturing capabilities for biologic therapeutics (large molecules) as we plan to use the premises for the manufacture of

materials for toxicology studies and drug substance for early human clinical studies with the goal of increasing flexibility and speed in advancing new investigational therapies into clinical trials;

- In April 2023, our collaboration partner Biogen exercised its option to develop and commercialize our ATV program targeting Amyloid Beta, triggering an option exercise payment of $5.0 million, which we received in May 2023;
- In April 2023, we presented final data from the 28-day treatment period of the Phase 1b study of DNL343 in participants with ALS at the 75th Annual Meeting of the American Academy of Neurology ("AAN"). The results continued to demonstrate that once-daily oral dosing with DNL343 for 28 days was generally well tolerated and demonstrated extensive CSF penetration. In addition, robust inhibition of biomarkers associated with the ISR pathway was observed in blood samples from study participants;
- In May 2023, the first patient was dosed with DNL343 in the Phase 2/3 HEALEY ALS Platform Trial. Recruitment of participants continues for this trial;
- In June 2023, in conjunction with Biogen, and based on review of portfolio timelines and resource prioritization, we announced plans to revise the clinical development program for BIIB122/DNL151. Prior to the planned revisions, the BIIB122 clinical development program encompassed two global late-stage clinical trials: the Phase 2b LUMA study in participants with early-stage Parkinson's disease, which commenced in May 2022; and the Phase 3 LIGHTHOUSE study in participants with Parkinson's disease related to LRRK2 mutations, which commenced in September 2022. In consideration of the LIGHTHOUSE study's complexity, including the long timeline with anticipated study completion in 2031, Biogen and we plan to refocus our efforts to enable a timely readout on efficacy in idiopathic early-stage Parkinson's disease while gaining further clinical data in Parkinson's disease with and without a LRRK2 mutation. The planned revisions to the BIIB122 clinical development program are not based on any safety or efficacy data from studies of BIIB122. Biogen and we plan to modify the LUMA study's enrollment criteria to allow for inclusion of eligible participants with Parkinson's disease and a confirmed pathogenic variant of LRRK2, in addition to continuing to enroll eligible participants with idiopathic early-stage Parkinson's disease. Collectively, data from the LUMA study will inform next steps for the development of BIIB122 in Parkinson's disease;
- In June 2023, we announced a robust reduction in Neurofilament Light ("NfL") with DNL310 treatment in MPS II (Hunter syndrome). Interim results demonstrated average reduction of 64% (p <0.001) from baseline in serum NfL after two years of dosing with DNL310 in the Phase 1/2 study. The FDA has recommended assessment of NfL, a marker of neuroaxonal damage, as a possible biomarker in MPS II;
- In July 2023, we presented additional healthy volunteer data from Part A of the Phase 1/2 study of TAK-594/DNL593 at the Alzheimer's Association International Conference, which continued to demonstrate that single doses of TAK-594/DNL593 resulted in substantial increases in CSF PGRN levels and were generally well tolerated. Recruitment of participants with symptomatic FTD-GRN loss of function mutations in Part B (ascending multiple doses) of the Phase 1/2 study is ongoing;
- In August 2023, 2024, we announced that Sanofi had completed enrollment in the Phase 2 HIMALAYA study in July; primary completion of the study is estimated to be January 2024. Further, in November 2023 we announced that Sanofi has completed enrollment of both the global Phase 2 HIMALAYA study in ALS and the Phase 2 study in MS;

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- In August 2023, we announced that Sanofi completed a Phase 2 study of eclitasertib, also known as SAR443122/DNL758, in patients with CLE in June. In October, Sanofi announced that the development of eclitasertib in CLE is being discontinued because the Phase 2 proof-of-concept study did not meet its primary endpoint (percent change from baseline in CLASI-A at week 12). Eclitasertib was found to be generally well-tolerated. Sanofi continues to recruit the Phase 2 study of eclitasertib in patients with UC;
- In August 2023 we announced that, in agreement with Takeda, the companies will discontinue clinical development of TAK-920/DNL919 in Alzheimer's disease. This is a strategic decision based on the totality of clinical data emerging from the single ascending dose Phase 1 study of TAK-920/DNL919 in healthy volunteers and in consideration of the rapidly evolving treatment landscape for Alzheimer's disease whereby an understanding of drug combinations with newly approved therapies will be important. A preliminary analysis of Phase 1 data indicates robust target engagement and effects on microglial biomarkers (e.g., CSF1R, SPP1, IL1RA, IP10, MIP1b, MCP-1), which were consistent with preclinical studies that demonstrate that ATV:TREM2 induces robust changes to a responsive microglial cell state (van Lengerich B, et al. Nat Neurosci. 2023). In the Phase 1 study, TAK-920/DNL919 was clinically well tolerated at doses with demonstrated changes in CSF biomarkers and there were no serious adverse events or severe treatment emergent adverse events; however, safety signals of moderate, reversible hematologic effects were observed at the highest dose tested, suggesting a narrow therapeutic window for the Alzheimer's disease patient population. The Phase 1 safety findings are believed to be specific to properties of TAK-920/DNL919 and TREM2 biology. Denali and Takeda will continue to focus research efforts on back-up molecules in preclinical development, including exploration of potential combination therapy given recent new drug approvals in Alzheimer's disease;
- In August 2023, we announced that the Investigational New Drug ("IND") application for DNL126 in MPS IIIA has been accepted and start-up activities for the Phase 1/2 study are ongoing;
- In August 2023, we presented new interim data from the Phase 1/2 study of DNL310 in MPS II in an oral presentation at the Society for the Study of Inborn Errors of Metabolism ("SSIEM") Annual Symposium 2023. The interim clinical outcomes data, safety profile, and biomarker effects, including normalization of CSF heparan sulfate and reduction in NfL, continue to support development of DNL310 in MPS II. Recruitment is ongoing in the global Phase 2/3 COMPASS study and is expected to be completed in 2024. In February, we presented new positive data from the ongoing Phase 1/2 study of DNL310 tividenofusp alfa in neuronopathic MPS II at the 20th Annual WORLD*Symposium*™ demonstrating sustained normalization of heparan sulfate in cerebrospinal fluid (CSF HS), robust and non-neuronopathic MPS II; sustained reductions in biomarkers of lysosomal dysfunction and neuronal damage (NfL; neurofilament light), and improvements and stabilization of multiple clinical outcomes measures over two years of treatment. Also in February, we participated in the Reagan-Udall Foundation for the FDA workshop on CSF HS as a potential surrogate biomarker to support accelerated approval in MPS. Based on continued dialogue with the Center for Drug Evaluation and Research (CDER) division of the FDA in April, we believe the division may be open to discussing an accelerated path for tividenofusp alfa. We look forward to continuing the productive dialogue with CDER and, in parallel, conducting the global Phase 2/3 COMPASS study;

- In August 2023, January 2024, we announced that Part B in the TAK-594/DNL593 Phase 1/2 study in participants with FTD-GRN had been voluntarily paused to implement protocol modifications and is expected to resume this year;

- In January 2024, we announced our intention to divest our preclinical small molecule portfolio, which was completed effective March 1, 2024. We will maintain ownership of, and continue to advance, our current portfolio of clinical stage small molecule programs. The decision was made based on clinical validation and prioritization of our TV-enabled platforms for brain delivery of large molecules;

- In February 2024, we announced that dosing had been initiated in the Phase 1/2 study of DNL126 in MPS IIIA; Phase 1/2 biomarker and safety data are expected by the end of 2024. Further, in February 2024, we presented supportive preclinical data at WORLDS*ymposium*™ demonstrating that DNL126 improves lysosomal and microglial morphology, degeneration, and cognitive behavior in MPS IIIA mice;

- In February 2024, we announced that the Phase 2 HIMALAYA study evaluating SAR443820/DNL788 in participants with ALS did not meet the primary endpoint of change in ALS Functional Rating Scale-Revised (ALSFRS-R). Sanofi intends to present the detailed efficacy and safety results of the ALS Phase 2 HIMALAYA study at a future scientific forum. Sanofi is evaluating SAR443820/DNL788 in another Phase 2 clinical trial in participants with MS which is fully enrolled, and the outcome of HIMALAYA study has no impact on the ongoing MS study;

- In February 2024, we announced that we entered into a securities purchase agreement with certain existing accredited investors for the private placement of 3,244,689 shares of our common stock at a price of $17.07 per share and pre-funded warrants to purchase an aggregate of 26,046,065 shares of our common stock at a purchase price of $17.06 per pre-funded warrant, resulting in net proceeds of approximately $499.3 million. The pre-funded warrants have an exercise price of $0.01 per share of Common Stock, and are immediately exercisable and will remain exercisable until exercised in full. The private placement closed on February 29, 2024, subject to customary closing conditions;

- In February 2024, we announced that we executed an amendment to the Definitive LRRK2 a Collaboration and License Development Funding Agreement in January 2024 with a third party related to a global Phase 2a study of BIIB122/DNL151, which we plan to solely operationalize to evaluate safety and Waiver biomarkers associated with BIIB122 in participants with Parkinson's disease and confirmed pathogenic variants of LRRK2. This agreement includes committed funding of $75.0 million, of which $12.5 million was received in January 2024, and Amendment the remainder will be triggered based on time and operational milestones in the study. The third party will be eligible to Right receive low single-digit royalties from Denali on annual worldwide net sales of First Negotiation (ROFN), Option, and License Agreement. As part LRRK2 inhibitors for the treatment of Parkinson's disease, with royalty amounts varying based on the scope of the amendment, certain milestone criteria were changed while label. We plan to initiate the total amount Phase 2a study in 2024. Biogen will continue to conduct the ongoing global Phase 2b LUMA study in early-stage Parkinson's disease. Denali and Biogen will co-commercialize BIIB122/DNL151 assuming regulatory approval; and

- In May 2024, the Sean M. Healey & AMG Center for ALS at Massachusetts General Hospital (MGH) in collaboration with the Northeast ALS Consortium (NEALS) announced that enrollment is complete in Regimen G (DNL343) of development, regulatory, and commercial milestones across all indications remains the same. In addition, Biogen agreed to waive the remaining option and rights of first negotiation under the ROFN and Option Agreement. Phase 2/3 HEALEY ALS Platform Trial.

We do not have any products approved for sale and have not generated any product revenue since our inception. We have funded our operations primarily from the issuance and sale of convertible preferred stock, the sale of common stock and pre-funded warrants to purchase shares of our common stock in public offerings and private placements, and payments received from our collaboration and funding agreements with Takeda, Sanofi, Biogen and Biogen. other third parties.

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We have incurred significant operating losses to date and expect to continue to incur operating losses for the foreseeable future. We had net losses of $99.4 million $101.8 million and $25.8 million $109.8 million for the three and nine months ended September 30, 2023, respectively. Our net losses were $103.3 million March 31, 2024 and $227.3 million for the three and nine months ended September 30, 2022 2023, respectively, respectively. . As of September 30, 2023 March 31, 2024, we had an accumulated deficit of $996.7 million $1.22 billion. Our ability to generate product revenue will depend on the successful development and eventual commercialization of one or more of our product candidates. We expect to continue to incur significant expenses and operating losses as we advance our current clinical stage programs through healthy volunteer and patient trials; broaden and improve our BBB platform technology; acquire, discover, validate and develop additional product candidates; obtain, maintain, protect and enforce our intellectual property portfolio; and hire additional personnel.

Components of Operating Results

Collaboration Revenue

To date, we have not generated any revenue from product sales and do not expect to generate any revenue from product sales for the foreseeable future. All revenue recognized to date has been collaboration and license revenue from our collaboration agreements with Takeda, Sanofi and Biogen.

Future revenue may be recognized from the Takeda Collaboration Agreement, Sanofi Collaboration Agreement, and Biogen Collaboration Agreement, and may be generated from product sales or milestone payments, royalties and profit sharing reimbursement from other collaboration agreements, strategic alliances and licensing arrangements. We expect that our revenue will fluctuate from quarter-to-quarter and year-to-year as a result of the timing and amount of license fees, option exercise fees, milestone payments, profit sharing reimbursement, other payments and product sales, to the extent any are successfully commercialized. If we fail to complete the development of our product candidates in a timely manner or obtain regulatory approval for them, our ability to generate future revenue, and our results of operations and financial position, would be materially adversely affected.

Operating Expenses

Research and Development

Research and development activities account for a significant portion of our operating expenses. We record research and development expenses as incurred. Research and development expenses incurred by us for the discovery and development of our product candidates and BBB platform technology include:

- external research and development expenses, including:
  - expenses incurred under arrangements with third parties, such as contract research organizations ("CROs"), preclinical testing organizations, contract development and manufacturing organizations ("CDMOs"), academic and non-profit institutions and consultants;
  - expenses to acquire technologies to be used in research and development that have not reached technological feasibility and have no alternative future use;
  - fees related to our license and collaboration agreements;
- personnel related expenses, including salaries, benefits and stock-based compensation expense; and
- other expenses, which include direct and allocated expenses for laboratory, facilities and other costs.

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A portion of our research and development expenses are direct external expenses, which we track on a program-specific basis once a program has commenced late-stage IND-enabling studies.

Program expenses include expenses associated with our most advanced product candidates and the discovery and development of backup or next-generation molecules. We also track external expenses associated with our TV platform. These expenses include external expenses incurred by us relating to our Takeda Collaboration Agreement, Sanofi Collaboration Agreement and Biogen Collaboration Agreement. All external costs associated with earlier stage programs, or that benefit the entire portfolio, are tracked as a group. We also incur personnel and other operating expenses for our research and development programs which are presented in aggregate. These expenses primarily relate to salaries and benefits, stock-based compensation, facility expenses including rent and depreciation, and lab consumables. Where we share costs with our collaboration partners, such as in our Biogen Collaboration Agreement and Takeda Collaboration Agreement, research and development expenses may include cost sharing reimbursements from, or payments to, our collaboration partners.

It is challenging to predict the nature, timing and estimated long-range costs of the efforts that will be necessary to complete the development of, and obtain regulatory approval for, any of our product candidates. This is made more challenging by events outside of our control, such as the COVID-19 pandemic and increased geopolitical uncertainty. We are also unable to predict when, if ever, material net cash inflows will commence from sales or licensing of our product candidates. This is due to the numerous risks and uncertainties associated with drug development, including the uncertainty of:

- our ability to add and retain key research and development personnel;
- our ability to establish an appropriate safety profile with IND-enabling toxicology studies;
- our ability to successfully develop, obtain regulatory approval for, and then successfully commercialize, our product candidates;
- our successful enrollment in and completion of clinical trials;
- the costs associated with the development of any additional product candidates we identify in-house or acquire through collaborations;
- our ability to discover, develop and utilize biomarkers to demonstrate target engagement, pathway engagement and the impact on disease progression of our molecules;
- our ability to establish agreements with third-party manufacturers for clinical supply for our clinical trials and commercial manufacturing, if our product candidates are approved;
- the terms and timing of any collaboration, license or other arrangement, including the terms and timing of any milestone payments thereunder;
- our ability to obtain and maintain patent, trade secret and other intellectual property protection and regulatory exclusivity for our product candidates if and when approved;

- our receipt of marketing approvals from applicable regulatory authorities;
- our ability to commercialize products, if and when approved, whether alone or in collaboration with others; and
- the continued acceptable safety profiles of the product candidates following approval.

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A change in any of these variables with respect to the development of any of our product candidates would significantly change the costs, timing and viability associated with the development of that product candidate. We expect our research and development expenses to increase at least over the next several years as we continue to implement our business strategy, advance our current programs, expand our research and development efforts, seek regulatory approvals for any product candidates that successfully complete clinical trials, access and develop additional product candidates and incur expenses associated with hiring additional personnel to support our research and development efforts. In addition, product candidates in later stages of clinical development generally incur higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials.

General and Administrative

General and administrative expenses include personnel related expenses, such as salaries, benefits, travel and stock-based compensation expense, expenses for outside professional services and allocated expenses. Outside professional services consist of legal, accounting and audit services and other consulting fees. Allocated expenses consist of rent, depreciation and other expenses related to our office and research and development facility not otherwise included in research and development expenses. We expect to increase our administrative headcount as we advance our product candidates through clinical development, which will increase our general and administrative expenses.

Gain from divestiture of small molecule programs

The gain from the divestiture of small molecule programs consists entirely of the non-cash gain associated with the divestiture of assets associated with select preclinical small molecule programs, including specified intellectual property, tangible assets and equipment used to conduct early stage small molecule drug discovery from the Company, in exchange for equity consideration.

Interest and Other Income, Net

Interest and other income, net, consists primarily of interest income and investment income earned on our cash, cash equivalents, and marketable securities, and as well as sublease income.

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Results of Operations

Comparison of the three and nine months ended September 30, 2023 March 31, 2024 and 2022 2023

The following table sets forth the significant components of our results of operations (in thousands):

	Three Months Ended March 31,		Three Months Ended March 31,	Ch
	2024			
Collaboration revenue:				
Collaboration revenue:				
Collaboration revenue:				
Collaboration revenue from customers				
Collaboration revenue from customers				
Collaboration revenue from customers	$ —	$ 35,141	$ (35,141)	*

	Three Months Ended September 30,		Change	
	2023	2022	$	%
Collaboration revenue:				
Collaboration revenue from customers	$ 1,267	$ 184	$ 1,083	* %
Other collaboration revenue	—	3,375	(3,375)	*
Total collaboration revenue	1,267	3,559	(2,292)	(64)
Operating expenses:				
Research and development	89,737	87,786	1,951	2
General and administrative	25,325	23,259	2,066	9
Total operating expenses	115,062	111,045	4,017	4
Loss from operations	(113,795)	(107,486)	(6,309)	6
Interest and other income, net	14,442	4,187	10,255	*
Loss before income taxes	(99,353)	(103,299)	3,946	(4)

Net loss	Net loss	$ (99,353)	$ (103,299)	$ 3,946	(4) %
Net loss				$ (101,802)	$ (109,781)	$ 7,979	(7)

* Percentage is not meaningful.

	Nine Months Ended September 30,		Change	
	2023	2022	$	%
Collaboration revenue:				
Collaboration revenue from customers	$ 330,531	$ 94,805	$ 235,726	* %
Other collaboration revenue	—	3,375	(3,375)	*
Total collaboration revenue	330,531	98,180	232,351	*
Operating expenses:				
Research and development	316,073	266,621	49,452	19
General and administrative	78,585	66,959	11,626	17
Total operating expenses	394,658	333,580	61,078	18
Loss from operations	(64,127)	(235,400)	171,273	(73)
Interest and other income, net	38,376	8,114	30,262	*
Loss before income taxes	(25,751)	(227,286)	201,535	(89)
Income tax expense	—	(27)	27	*
Net loss	$ (25,751)	$ (227,313)	$ 201,562	(89) %

* Percentage is not meaningful.

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Collaboration revenue. Collaboration There was no collaboration revenue was $1.3 million and $330.5 million for the three and nine months ended September 30, 2023, respectively, March 31, 2024 and $3.6 million and $98.2 million collaboration revenue of $35.1 million for the three and nine months ended September 30, 2022 March 31, 2023. The decrease in revenue of $2.3 million for the three months ended September 30, 2023 compared to the three months ended September 30, 2022 was primarily due to a decrease of revenue earned under the Sanofi Collaboration of $3.4 million, partially offset by an increase of $1.1 million in revenue earned under the Biogen Collaboration Agreement due to the August 2023 amendment which resulted in the satisfaction of the only remaining performance obligation for the second option program. The increase in collaboration revenue of $232.3 million for the nine months ended September 30, 2023 compared to the nine months ended September 30, 2022 was primarily due to $293.9 million in revenue recognized in April 2023 under the Biogen Collaboration Agreement as a result of Biogen exercising its option to license our ATV:Abeta program, partially offset by a decrease of $41.9 million in revenue earned under the Takeda Collaboration Agreement, as well as a decrease of $18.4 million in milestone revenue earned under the Sanofi Collaboration Agreement. The decreases in revenues from the Sanofi $25.0 million and Takeda Collaboration Agreements are due to the timing of underlying activities and achievement of milestones under the collaboration agreements. $10.0 million.

Research and development expenses. Research and development expenses were $89.7 million $107.0 million and $316.1 million $128.8 million for the three and nine months ended September 30, 2023, compared to $87.8 million March 31, 2024 and $266.6 million for the three and nine months ended September 30, 2022, 2023, respectively.

The following table summarizes our research and development expenses by program and category (in thousands):

		Three Months Ended September 30,		Nine Months Ended September 30,	
		2023	2022	2023	2022
		Three Months Ended March 31,			
		Three Months Ended March 31,			
		Three Months Ended March 31,			
		2024			
		2024			
		2024			
ETV:IDS program external expenses	ETV:IDS program external expenses	$ 20,388	$ 12,610	$ 87,674	$ 47,743

ETV:IDS program external expenses					
ETV:IDS program external expenses					
ETV:SGSH program external expenses					
ETV:SGSH program external expenses					
ETV:SGSH program external expenses					
PTV:PGRN program external expenses					
PTV:PGRN program external expenses					
PTV:PGRN program external expenses	PTV:PGRN program external expenses	1,889	3,838	8,107	12,632
TV platform and other program external expenses	TV platform and other program external expenses	3,836	8,038	18,090	25,889
TV platform and other program external expenses					
TV platform and other program external expenses					
LRRK2 program external expenses					
LRRK2 program external expenses					
LRRK2 program external expenses	LRRK2 program external expenses	1,049	7,099	3,867	17,387
eIF2B program external expenses	eIF2B program external expenses	4,971	4,415	14,866	11,174
eIF2B program external expenses					
eIF2B program external expenses					
Other external research and development expenses					
Other external research and development expenses					
Other external research and development expenses	Other external research and development expenses	6,512	8,314	20,031	26,182
Personnel related expenses(1)	Personnel related expenses(1)	39,578	35,967	119,640	107,111
Personnel related expenses(1)					
Personnel related expenses(1)					
Other unallocated research and development expenses	Other unallocated research and development expenses	10,931	9,967	38,693	27,963
Net cost sharing payments (reimbursements)(2)		583	(2,462)	5,105	(9,460)
Other unallocated research and development expenses					
Other unallocated research and development expenses					
Net cost sharing payments(2)					
Net cost sharing payments(2)					
Net cost sharing payments(2)					
Total research and development expenses	Total research and development expenses	$ 89,737	$ 87,786	$ 316,073	$ 266,621
Total research and development expenses					
Total research and development expenses					

(1) Personnel related expenses include stock-based compensation expense of $15.8 million $16.3 million and $47.8 million $16.8 million for the three and nine months ended September 30, 2023, respectively, March 31, 2024 and $14.7 million and $45.1 million for the three and nine months ended September 30, 2022, respectively, reflecting an increase of $1.1 million and $2.7 million, 2023, respectively.

(2) There were $0.6 million and $5.1 million in net Net cost sharing payments during details are broken down as shown in the three table below. The underlying costs for reimbursements are included with the specified external expenses line and nine months ended September 30, 2023, respectively, consisting of $3.4 million and $14.5 million, respectively, owed to Biogen for LRRK2 personnel related expenses in the table above. ATV:TREM2 program external expenses and program internal expenses (included are presented within Personnel related expenses), partially offset by $1.7 million and $5.1 million, respectively, of reimbursements from Takeda for the PTV:PGRN program (included within PTV program external program expenses and Personnel related expenses), and $1.1 million and $4.3 million respectively, of reimbursements from Takeda for the ATV:TREM2 program (included within TV platform and other program external expenses and Personnel related expenses). For the three and nine months ended September 30, 2022, net cost sharing reimbursements includes reimbursements from Takeda for the PTV:PGRN program (included within PTV:PGRN program external program expenses and Personnel related expenses) of $2.3 million and $8.0 million, respectively, and reimbursements from Takeda for the ATV:TREM2 program (included within TV Platform and other program external expenses and Personnel related expenses) of $1.6 million and $5.2 million, respectively. For the three and nine months ended September 30, 2022, cost sharing reimbursements were partially offset by cost sharing payments of $1.4 million and $3.8 million, respectively, owed to Biogen. line.

	Three Months Ended March 31,	
	2024	2023
Takeda: net reimbursements for ATV:TREM2 program	$ (513)	$ (1,657)
Takeda: net reimbursements for PTV:PGRN program	(1,200)	(1,478)
Biogen: net payments for LRRK2 program	4,789	4,150
Net cost sharing payments (reimbursements)	$ 3,076	$ 1,015

The increase decrease in research and development expenses of approximately $1.9 million $21.8 million for the three months ended September 30, 2023 March 31, 2024 compared to the three months ended September 30, 2022, was primarily attributable to the following:

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- An increase of $7.8 million in ETV:IDS program external expenses reflecting the continued progress of this program in clinical trials during 2023, including costs related to our ongoing Phase 1/2 study and our potentially registrational Phase 2/3 study;
- An increase of $0.6 million in eIF2B program external expenses reflecting the continued progress of this program in clinical trials during 2023;
- An increase of $3.6 million in personnel related expenses, consisting of $2.5 million in employee compensation and $1.1 million in stock-based compensation expense pertaining to additional salaries, related expenses, and equity award grants driven by an increase in our research and development headcount; and
- An increase of $3.0 million in net cost sharing payments due to the transition of LRRK2 clinical activities to Biogen, resulting in cost sharing reimbursements flipping to payments.

These increases were partially offset by decreases of $6.1 million in LRRK2 program external expenses due to the transition of LRRK2 clinical activities to Biogen, $4.2 million in TV platform and other program external expenses as a result of discontinuation of development of DNL919, $1.9 million in PTV:PGRN program external expenses due to the timing of significant external research and manufacturing related activities year over year, and $1.8 million in other external research and development expenses.

The increase in research and development expenses of approximately $49.5 million for the nine months ended September 30, 2023 compared to the nine months ended September 30, 2022 March 31, 2023, was primarily attributable to the following:

- An increase a decrease of $39.9 million $16.9 million in ETV:IDS program external expenses primarily due to because the first quarter of 2023 included expense for a contingent consideration payment of $30.0 million recorded in the first quarter of 2023 $30.0 million related to the acquisition of F-star Gamma, which was triggered in March 2023 upon the achievement of a specified clinical milestone in the ETV:IDS program;
- An increase of $10.7 million in other unallocated research and development expenses primarily due to program. This decrease was partially offset by increased facility costs as a result of accelerated depreciation on leasehold improvements associated with the termination of the SLC Lease as well as other general research costs;
- An increase of $3.7 million in eIF2B program external expenses reflecting spend from the continued progress of this program in clinical trials during 2023; in 2024, including costs related to our ongoing Phase 1/2 study and our potentially registrational Phase 2/3 study;
- An increase decreases of $12.5 million $1.9 million and $1.2 million in personnel related TV platform and other program external expenses consisting of $9.8 million in employee compensation and $2.7 million in stock-based compensation expense pertaining to additional salaries, related including ATV:TREM2 expenses, and equity award grants driven by an increase PTV:PGRN program external expenses, respectively, due to the discontinuation of clinical development of TAK-920/DNL919 (ATV:TREM2) in our research Alzheimer's disease and development headcount; and voluntary pause of Part B in the TAK-594/DNL593 (PTV:PGRN) Phase 1/2 study, respectively;
- An increase a decrease of $14.6 million in net cost sharing payments primarily due to the transition of LRRK2 clinical activities to Biogen, resulting in cost sharing reimbursements flipping to payments.

These increases were partially offset by decreases of $13.5 million $1.3 million in LRRK2 program external expenses due to the transition of LRRK2 clinical activities to Biogen, $7.8 million in TV platform Biogen; and other program external expenses as

- a result decrease of discontinuation of development of DNL919, $6.1 million $1.9 million in other external research and development expenses expenses.

These decreases were partially offset by increases of $2.9 million and $4.5 million $1.8 million in PTV:PGRN eIF2B and ETV:SGSH program external expenses, respectively, reflecting the continued progress of these programs in clinical trials during 2024, and an increase of $2.1 million in net cost sharing payments due to increased payments due to Biogen as a result of increased LRRK2 clinical trial costs incurred by Biogen, offset by decreased reimbursements from Takeda as a result of the timing discontinuation of significant external research TREM2 DNL919 phase 1 trial and manufacturing related activities year over year.

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TAK-594/DNL593.

General and administrative expenses. General and administrative expenses were $25.3 25.2 million for the three months ended September 30, 2023 March 31, 2024 compared to $23.3 $27.1 million for the three months ended September 30, 2022 March 31, 2023. The increase decrease of $2.0 million $1.9 million was primarily attributable to to a $3.0 million increase $2.4 million of combined decreases in personnel-related expenses consisting of employee compensation professional services, facilities and stock-based compensation

expense associated with additional salary expenses and equity award grants driven by higher general and administrative headcount, other corporate costs, partially offset by a $1.0 million decrease in professional services and other corporate costs.

General and administrative expenses were $78.6 million for the nine months ended September 30, 2023 compared to $67.0 million for the nine months ended September 30, 2022. The increase of $11.6 million was primarily attributable to the following:

- $8.0 million $0.5 million of increased personnel-related expenses consisting of employee compensation and stock-based compensation expense associated with additional salary expenses and equity award grants driven by higher general and administrative headcount; and expense.

• *Gain from divestiture of small molecule programs.* $3.6 million For a full description, see Item 2. Components of combined increases Operating Results included in professional services, facilities and other corporate costs. this Quarterly Report on Form 10-Q.

Liquidity and Capital Resources

Sources of Liquidity

As of March 31, 2024, we had cash, cash equivalents and marketable securities in the amount of $1.43 billion. We fund our operations primarily with the proceeds from the sale of common stock in public offerings and payments received from our collaboration partners, including those received under agreements with Takeda, Sanofi, and Biogen.

In our January 2020 follow-on offering, we We have sold 9.0 million shares of common stock (inclusive of shares sold pursuant to an overallotment option granted to the underwriters and other securities in connection public offerings, a private placement, and stock purchase agreements with the offering) through an underwritten public offering at a price of $23.00 per share for Takeda and Biogen.

Through March 31, 2024 we have obtained aggregate net proceeds of approximately $193.9 million $754.4 million from public offerings of our common stock, including $296.2 million obtained through the sale of 11.9 million shares of common stock in October 2022. Under stock purchase agreements with collaboration partners we have received a further $575.0 million through March 31, 2024.

Further, in February 2024 we received net proceeds of approximately $499.3 million from our private placement through the sale of approximately 3.2 million shares of common stock andpre-funded warrants to purchase approximately 26.0 million shares of our common stock.

In February 2022, we established a registered “at-the-market” facility for the sale of up to $400.0 million of shares of common stock from time to time by entering into an equity distribution agreement with Goldman Sachs & Co. LLC, SVB Securities LLC and Cantor Fitzgerald & Co. as sales agents. To date, no shares have been sold under the equity distribution agreement.

In October 2022, we sold 11.9 million shares of common stock (inclusive of shares sold pursuant to an overallotment option granted to the underwriters in connection with the offering) through an underwritten public offering at a price of $26.50 per share for aggregate net proceeds of approximately $296.2 million.

Pursuant to our collaboration and research funding agreements with Takeda, Sanofi, Biogen and Biogen, an unrelated third party, through September 30, 2023 March 31, 2024 we have received upfront, option and milestone payments of $115.0 million, $225.0 million, $565.0 million and $565.0 million $12.5 million, respectively, and have also received $38.5 43.9 million and $16.2 million of gross cost sharing reimbursements from Takeda and Biogen, respectively, and received $13.7 million of reimbursement in specified reimbursements from Sanofi for the Phase 1b trial for DNL747 for ALS and associated activities. Sanofi.

Further, under associated stock purchase agreements with Takeda and Biogen, through September 30, 2023 we have received $110.0 million and $465.0 million, respectively, for the sale and issuance of shares of our common stock to these collaboration partners.

As of September 30, 2023, we had cash, cash equivalents and marketable securities in the amount of $1.12 billion.

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Future Funding Requirements and Commitments

To date, we have not generated any product revenue. We do not expect to generate any product revenue unless and until we obtain regulatory approval of and commercialize any of our product candidates, and we do not know when, or if, either will occur.

We expect to continue to incur significant losses for the foreseeable future, and we expect the losses to increase as we expand our research and development activities and continue the development of, and seek regulatory approvals for, our product candidates, and begin to commercialize any approved products. Further, we expect general and administrative expenses to increase as we continue to incur additional costs associated with supporting our growing operations. We are subject to all of the risks typically related to

the development of new product candidates, and we may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business. We anticipate that we will need substantial additional funding in connection with our continuing operations.

Until we can generate a sufficient amount of revenue from the commercialization of our product candidates or from our existing collaboration agreements, or future agreements with other third parties, if ever, we expect to finance our future cash needs through public or private equity or debt financings. Additional capital may not be available on reasonable terms, if at all. If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may have to significantly delay, scale back or discontinue the development or commercialization of one or more of our product candidates. If we raise additional funds through the issuance of additional debt or equity securities, it could result in dilution to our existing stockholders, increased fixed payment obligations and the existence of securities with rights that may be senior to those of our common stock. If we incur indebtedness, we could become subject to covenants that would restrict our operations and potentially impair our competitiveness, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. Additionally, any future collaborations we enter into with third parties may provide capital in the near term but limit our potential cash flow and revenue in the future. Any of the foregoing could significantly harm our business, financial condition and prospects.

Since our inception, we have incurred significant losses and negative cash flows from operations. We have an accumulated deficit of $996.7 million $1.22 billion through September 30, 2023 March 31, 2024. We expect to incur substantial additional losses in the future as we conduct and expand our research and development activities. We believe that our existing cash, cash equivalents and marketable securities will be sufficient to enable us to fund our projected operations through at least the twelve months following the filing date of this Quarterly Report on Form 10-Q, including our existing commitments as outlined below. We have based this estimate on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we currently expect. In the longer term, we anticipate that we will need substantial additional resources to fund our operations and meet future commitments.

Our existing commitments primarily relate to our obligations under existing lease agreements, and certain clinical and manufacturing agreements, including the DMSA with Lonza Sales AG ("Lonza") for the development and manufacture of biologic products. As of September 30, 2023 March 31, 2024, operating lease liabilities were $53.9 million $50.5 million. Under the SLC lease which was executed in April 2023, we have future undiscounted lease payments totaling approximately $13.4 million. Under the DMSA with Lonza, and certain other clinical and manufacturing agreements, we had total non-refundable purchase commitments as of September 30, 2023 March 31, 2024 of $87.7 million $67.6 million, with certain amounts subject to cost sharing with Takeda. While the lease obligations span multiple years, the majority of the purchase commitments with Lonza and other clinical and manufacturing agreements are due within twelve months, with some spanning several years. These commitments are more fully described in Note 7 6 - Commitments and Contingencies of our unaudited condensed consolidated financial statements included in this Quarterly Report on Form 10-Q. 10-Q.

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Our future funding requirements, including changes to and new commitments, will depend on many factors, including:

- the timing and progress of preclinical and clinical development activities;
- the number and scope of preclinical and clinical programs we decide to pursue;
- the progress of the development efforts of third parties with whom we have entered into license and collaboration agreements;
- our ability to maintain our current research and development programs and to establish new research and development, license or collaboration arrangements;
- our ability and success in securing manufacturing relationships with third parties or in establishing and operating a manufacturing facility;
- the costs involved in prosecuting, defending and enforcing patent claims and other intellectual property claims;
- the cost and timing of regulatory approvals;
- our efforts to enhance operational, financial and information management systems and hire additional personnel, including personnel to support development of our product candidates; and
- the costs and ongoing investments to in-license and/or acquire additional technologies.

A change in the outcome of any of these or other variables with respect to the development of any of our product candidates could significantly change the costs and timing associated with the development of that product candidate. Furthermore, our operating plans may change in the future, and we may need additional funds to meet operational needs and capital requirements associated with such operating plans.

Cash Flows

The following table sets forth a summary of the primary sources and uses of cash for each of the periods presented below (in thousands):

		Nine Months Ended September 30,			
		2023	2022		
	Three Months Ended March 31,			Three Months Ended March 31,	
	2024			2024	2023
Net cash used in operating activities	Net cash used in operating activities	$ (259,334)	$ (172,053)		
Net cash provided by (used in) investing activities		176,261	(13,828)		
Net cash used in investing activities					
Net cash provided by financing activities	Net cash provided by financing activities	13,115	11,019		
Net decrease in cash, cash equivalents and restricted cash	Net decrease in cash, cash equivalents and restricted cash	$ (69,958)	$ (174,862)		

Net Cash Used In Operating Activities

During the nine three months ended September 30, 2023 March 31, 2024, net cash used in operating activities was $259.3 million $113.6 million, which consisted of a net loss of $25.8 million $101.8 million, adjusted by non-cash items primarily related to stock-based compensation expense, depreciation and amortization, net amortization of discounts premiums and (discounts) on marketable securities, and non-cash rent expenses. expenses, and the non-cash gain on divestiture of small molecule programs. Cash used in operating activities was also driven by changes in our operating assets and liabilities, such as the reduction most significant of which was an increase in our related-party contract liability as a result of Biogen's option exercise other non-current assets related to costs associated with the new Salt Lake City manufacturing facility during the second quarter of 2023, as well as $30.0 million in contingent consideration payments to F-star during the nine three months ended September 30, 2023 March 31, 2024.

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Net Cash Provided By (Used In) Used In Investing Activities

During the nine three months ended September 30, 2023 March 31, 2024, net cash provided by used in investing activities was $176.3 million $453.2 million, which consisted of $1.6 billion $834.2 million of purchases of marketable securities, partially offset by $383.1 million in proceeds from maturities and sales of marketable securities, partially offset by $1.4 billion of purchases of marketable securities, and $10.7 million $2.2 million of capital expenditures to purchase property and equipment.

Net Cash Provided By Financing Activities

During the nine three months ended September 30, 2023 March 31, 2024, cash provided by financing activities was $13.1 $500.3 million which consisted of $499.3 million of net proceeds from the sale of common stock and pre-funded warrants in a private placement in February 2024, as well as proceeds from the exercise of options to purchase

common stock and purchases of ESPP shares. stock.

Critical Accounting Estimates

This discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with U.S. GAAP. The preparation of these consolidated financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the consolidated financial statements, as well as the reported revenues recognized and expenses incurred during the reporting periods. Our estimates are based on our historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions. Our significant accounting policies are described in detail in the notes to our consolidated financial statements included elsewhere in this report. In our "Management's Discussion and Analysis of Financial Condition and Results of Operations" included in our Annual Report on Form 10-K for the year ended December 31, 2022 December 31, 2023, as filed with the SEC on February 27, 2023, 28, 2024, we described the accounting estimates that we believe involve a significant level of estimation uncertainty which could have a material impact on our financial condition or results of operations. There have been no material changes to these critical accounting estimates during the nine three months ended September 30, 2023. March 31, 2024.

Recent Accounting Pronouncements

There have been no new accounting pronouncements or changes to accounting pronouncements during the nine three months ended September 30, 2023 March 31, 2024, as compared to the recent accounting pronouncements described in our Annual Report on Form 10-K for the year ended December 31, 2022 December 31, 2023, as filed with the SEC on February 27, 2023 February 28, 2024, that are of significance or potential significance to us.

ITEM 3. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

We are exposed to market risks in the ordinary course of our business, primarily related to interest rate and foreign currency sensitivities.

Interest Rate Sensitivity

We are exposed to market risk related to changes in interest rates. We had cash, cash equivalents and marketable securities of $1.12 billion $1.43 billion as of September 30, 2023 March 31, 2024, which consisted primarily of money market funds and marketable securities, largely composed of investment grade, short to intermediate term fixed income securities.

The primary objective of our investment activities is to preserve capital to fund our operations. We also seek to maximize income from our investments without assuming significant risk. To achieve our objectives, we maintain a portfolio of investments in a variety of securities of high credit quality and short-term duration, according to our board-approved investment policy. Our investments are subject to interest rate risk and could fall in value if market interest rates increase. A hypothetical 10% relative change in interest rates during any of the periods presented would not have had a material impact on our condensed consolidated financial statements.

Foreign Currency Sensitivity

The majority of our transactions occur in U.S. dollars. However, we do have certain transactions that are denominated in currencies other than the U.S. dollar, primarily the Euro, Swiss Franc and British Pound, and we therefore are subject to foreign exchange risk. The fluctuation in the value of the U.S. dollar against other currencies affects the reported amounts of expenses, assets and liabilities primarily associated with a limited number of preclinical, clinical and manufacturing activities.

ITEM 4. CONTROLS AND PROCEDURES

Evaluation of Disclosure Controls and Procedures

Our management has performed an evaluation of the effectiveness of the design and operation of our disclosure controls and procedures as defined in Rules 13a-15(e) and 15d-15(e) of the Exchange Act. Our disclosure controls and procedures are designed to ensure that information required to be disclosed in the reports 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, and that such information is accumulated and communicated to our management, including the Chief Executive Officer and the Chief Operating and Financial Officer, to allow timely decisions regarding required disclosures.

Any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objective and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on this evaluation, our Chief Executive Officer and Chief Operating and Financial Officer concluded that, as of September 30, 2023 March 31, 2024, the design and operation of our disclosure controls and procedures were effective at a reasonable assurance level.

Changes in Internal Control over Financial Reporting

There was no change in our internal control over financial reporting identified in connection with the evaluation required by Rule 13a-15(d) and 15d-15(d) of the Exchange Act that occurred during the quarter ended September 30, 2023 March 31, 2024 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

PART II. OTHER INFORMATION

ITEM 1. LEGAL PROCEEDINGS

From time to time, we may become involved in litigation or other legal proceedings. We are not currently a party to any litigation or legal proceedings that, in the opinion of our management, are likely to have a material adverse effect on our business. Regardless of outcome, litigation can have an adverse impact on us because of defense and settlement costs, diversion of management attention and resources and other factors.

ITEM 1A. RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the risks described below, as well as the other information in this Quarterly Report on Form 10-Q, including our financial statements and the related notes and the section titled "Management's Discussion and Analysis of Financial Condition and Results of Operations." The occurrence of any of the events or developments described below could harm our business, financial condition, results of operations and growth prospects. In such an event, the market price of our common stock could decline and you may lose all or part of your investment. Additional risks and uncertainties not presently known to us or that we currently deem immaterial also may impair our business operations and the market price of our common stock.

Risk Factor Summary

The This summary of risks below provides an overview of the principal risks we are exposed to. These risks are described more fully in the section entitled "Risk Factors" in this Quarterly Report on Form 10-Q.

Risks Related to Our Business, Financial Condition and Capital Requirements

- We are in the clinical stages of drug development and have a limited operating history and no products approved for commercial sale, which may make it difficult to evaluate our current business and predict our future success and viability.
- We have incurred significant net losses since our inception and anticipate that we will continue to incur net losses for the foreseeable future.
- Drug development is a highly uncertain undertaking. We have never generated any revenue from product sales, and may never do so.
- Due to the significant resources required for the development of our programs, and depending on our ability to access capital, we must prioritize development of certain product candidates.
- A pandemic, epidemic, or outbreak of an infectious disease, such as COVID-19, or the perception of its effects, may materially and adversely affect our business, operations, and financial condition.

Risks Related to the Discovery, Development and Commercialization of Our Product Candidates

- We are heavily dependent on the successful development of our BBB technology and the programs currently in our pipeline, which are in the preclinical and clinical development stages.
- We may not be successful in our efforts to continue to create a pipeline of product candidates or to develop commercially successful products.
- We have concentrated a substantial portion of our efforts on the treatment of neurodegenerative and lysosomal storage diseases a field, fields that has have seen limited success in drug development.
- We may encounter substantial delays in our clinical trials, or may not be able to conduct or complete our clinical trials on the timelines we expect, if at all.
- We may encounter difficulties enrolling and/or retaining patients in our clinical trials, and our clinical development activities could thereby be delayed or otherwise adversely affected.

- Our clinical trials may reveal significant adverse events, toxicities, or other side effects and may fail to demonstrate substantial evidence of the safety and efficacy or potency of our product candidates, which would prevent, delay or limit the scope of regulatory approval and commercialization.
- We face significant competition and there is a possibility that our competitors operating results may achieve regulatory approval before us or develop therapies that are safer or more effective than ours.
- The manufacture of our product candidates, particularly those that utilize our BBB platform technology, is complex and suffer if we may encounter difficulties in production. fail to compete effectively.
- If we are unable to establish sales and marketing capabilities or enter into agreements with third parties, we may not be successful in commercializing product candidates if and when they are approved.
- If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of our product candidates.

Risks Related to Regulatory Approval and Other Legal Compliance Matters

- The regulatory approval processes of the FDA, European Medicines Agency ("EMA") and comparable foreign regulatory authorities are lengthy, time consuming, and inherently unpredictable. If we are ultimately unable to obtain regulatory approval for our product candidates, we will be unable to generate product revenue.
- We currently conduct clinical trials outside the United States, and the FDA, EMA and applicable foreign regulatory authorities may not accept data from such trials.
- To the extent we seek orphan drug designation for any of our product candidates, we may be unable to obtain such designations or to maintain the benefits associated with orphan drug status.
- Healthcare legislative measures aimed at reducing healthcare costs may have a material adverse effect on our business and results of operations.
- Our business is subject to complex and evolving U.S. and foreign laws and regulations, information security policies, and contractual obligations relating to privacy and data protection.

Risks Related to Our Reliance on Third Parties

- We depend on collaborations with third parties for the research, development and commercialization of certain product candidates. If any such collaborations are not successful, we may not be able to realize the market potential of those product candidates.

- We rely on third parties to conduct our clinical trials and some aspects of our research and preclinical testing, and those third parties may not perform satisfactorily.
- We contract with Our reliance on third parties for the manufacture of the significant majority of the materials for our research programs, preclinical studies and clinical trials. This reliance on third parties may increase the risk that we will not have sufficient quantities of such materials or product candidates.
- We depend on third-party suppliers for key raw materials used in our manufacturing, and the loss of these suppliers or their inability to supply us with adequate raw materials could harm our business.

Risks Related to Our Intellectual Property

- If we are unable to obtain and maintain patent protection for our product candidates or our BBB technology, our competitors could develop and commercialize products or technology similar or identical to ours, and adversely affect our ability to commercialize any product candidates.
- If any of our owned or in-licensed patent applications do not issue as patents in any jurisdiction, we may not be able to compete effectively.
- Our rights to develop and commercialize our BBB technology and product candidates are subject, in part, to the terms of licenses granted to us by others or licenses granted by us to others.
- We may not be able to protect our intellectual property and proprietary rights throughout the world.
- Our patent protection could be reduced or eliminated if we are unable to comply with requirements imposed by government patent agencies.
- Changes in U.S. patent law could impair our ability to protect our products.
- Our patent protection could be compromised if we are unable to comply with requirements imposed by government patent agencies.
- Issued patents covering our BBB technology, product candidates and other technologies could be found invalid or unenforceable if challenged.
- Patent terms may be inadequate to protect our competitive position on our product candidates for an adequate amount of time.
- We may be subject to claims challenging the inventorship of our intellectual property.
- If we are unable to protect the confidentiality of our trade secrets, our business would be harmed.
- We may not be successful in obtaining, through acquisitions, in-licenses, or otherwise, necessary rights to our BBB platform technology, product candidates or other technologies.
- We may be subject to claims that our employees, consultants, or advisors have wrongfully used or disclosed alleged trade secrets of their current or former employers.
- Third party Third-party intellectual property claims against us, our licensors or our collaborators may prevent or delay the development of our BBB platform technology, product candidates and other technologies.

Risks Related to Our Operations

- If we are not successful in attracting, motivating and retaining highly qualified personnel, we may not be able to successfully implement our business strategy.

- We have engaged in and may in the future engage in acquisitions or strategic partnerships, which may increase our capital requirements, dilute our stockholders, or cause us to incur debt or assume contingent liabilities.
- Our internal computer systems, or those used by our collaborators, CROs or other contractors, may fail or suffer security breaches or incidents that could compromise the confidentiality, integrity, and availability of such systems and data, and expose us to liability, and affect our reputation.
- Our business is subject to risks associated with international operations.

Risks Related to Ownership of Our Common Stock

- The market price of our common stock has been and may continue to be volatile, which could result in substantial losses for investors.
- If securities analysts publish negative evaluations of our stock, or if they do not publish research or reports about our business; the price of our stock and trading volume could decline.
- Raising additional capital may cause dilution to our existing stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates.
- Delaware law and provisions in our charter documents might prevent a change in control of our company or changes in our management, depressing the trading price of our common stock.
- Our amended and restated certificate of incorporation provides exclusive forums for disputes between us and our stockholders, limiting their ability to obtain a favorable judicial forum.

Risks Related to Our Business, Financial Condition and Capital Requirements

We are in the clinical stages of drug development and have a limited operating history and no products approved for commercial sale, which may make it difficult to evaluate our business and predict our future success and viability.

We are a clinical-stage biopharmaceutical company with a limited operating history, focused on developing therapeutics for neurodegenerative diseases, including Alzheimer's disease, Parkinson's disease, and ALS. ALS, and lysosomal storage diseases, including Hunter syndrome and Sanfilippo syndrome. We commenced operations in May 2015, have no products approved for commercial sale, and have not generated any revenue from product sales. Drug development is a highly uncertain undertaking and involves a substantial degree of risk. Our clinical-stage programs are in various phases ranging from Phase 1 through Phase 3. We have not initiated clinical trials for any of our other current product candidates. To date, we have not completed a pivotal clinical trial, obtained marketing approval for any product candidates, manufactured a commercial scale product or arranged for a third party to do so on our behalf, or conducted sales and marketing activities necessary for successful product commercialization. Our limited operating history makes any assessment of our future success and viability subject to significant uncertainty. We will encounter risks and difficulties frequently experienced by clinical-stage biopharmaceutical companies, and we have not yet demonstrated an ability to successfully overcome such risks and difficulties. If we do not address these risks and difficulties successfully, our business will suffer.

We have incurred significant net losses since our inception and anticipate that we will continue to incur net losses for the foreseeable future.

We have incurred significant net losses since our inception. Our net losses were $99.4 101.8 million and $25.8 million $109.8 million for the three and nine months ended September 30, 2023, respectively. We had net losses of $103.3 million March 31, 2024 and $227.3 million for the comparable three and nine month periods ended September 30, 2022, 2023, respectively. As of September 30, 2023 March 31, 2024, we had an accumulated deficit of $996.7 million 1.22 billion.

We have invested significant financial resources in research and development activities, including for our preclinical and clinical product candidates and our TV platform. We do not expect to generate revenue from product sales for several years, if at all. The amount of our future net losses will depend, in part, on the level of our future expenditures and revenue. Moreover, our net losses may fluctuate significantly from quarter to quarter and year to year, such that a period-to-period comparison of our results of operations may not be a good indication of our future performance.

We expect to continue to incur significant expenses and increasingly higher operating losses for the foreseeable future. We anticipate that our expenses will increase substantially if and as we:

- continue our research and discovery activities;
- progress our current and any future product candidates through preclinical and clinical development;
- initiate and conduct additional preclinical, clinical, or other studies for our product candidates;
- work with our contract manufacturers to scale up the manufacturing processes for our product candidates or in the future, establish and operate a manufacturing facility;
- change or add additional contract manufacturers or suppliers;
- seek regulatory approvals and marketing authorizations for our product candidates;

- establish sales, marketing and distribution infrastructure to commercialize any products for which we obtain approval;

- acquire or in-license product candidates, intellectual property and technologies;

- make milestone, royalty or other payments due under any license or collaboration agreements;
- obtain, maintain, protect, and enforce our intellectual property portfolio, including intellectual property obtained through license agreements;
- attract, hire, and retain qualified personnel and incur increased stock-based compensation, especially in light of a competitive compensation environment;
- provide additional internal infrastructure to support our continued research and development operations and any planned commercialization efforts in the future;
- implement additional internal systems and infrastructure related to cybersecurity;
- experience any delays or encounter other issues related to our operations;
- meet the requirements and demands of being a public company;
- defend against any product liability claims or other lawsuits related to our products; and
- build clinical manufacturing capabilities and capacity.

Our prior losses and expected future losses have had and will continue to have an adverse effect on our stockholders' equity and working capital. In any particular quarter or quarters, our operating results could be below the expectations of securities analysts or investors, which could cause our stock price to decline.

Drug development is a highly uncertain undertaking and involves a substantial degree of risk. We have never generated any revenue from product sales, and we may never generate product revenue or be profitable.

We have no products approved for commercial sale and have not generated any revenue from product sales. To obtain revenue from the sales of our product candidates that are significant or large enough to achieve profitability, we must succeed, either alone or with third parties, in developing, obtaining regulatory approval for, manufacturing, and marketing therapies with significant commercial success.

Our ability to generate revenue and achieve profitability depends significantly on many factors, including:

- successfully prioritizing and completing research and preclinical and clinical development of our product candidates;
- obtaining regulatory approvals and marketing authorizations for product candidates for which we successfully complete clinical development and clinical trials;
- developing a sustainable and scalable manufacturing process for our product candidates, including those that utilize our TV platform, as well as establishing and maintaining commercially viable supply relationships with third parties that can provide adequate products and services to support clinical activities and commercial demand of our product candidates;
- identifying, assessing, acquiring and/or developing new product candidates;
- negotiating favorable terms in any collaboration, licensing or other arrangements into which we may enter;

- launching and successfully commercializing product candidates for which we obtain regulatory and marketing approval, either by collaborating with a partner or, if launched independently, by establishing a sales, marketing and distribution infrastructure;

- obtaining and maintaining an adequate price for our product candidates, both in the United States and in foreign countries where our products are commercialized;
- obtaining adequate reimbursement for our product candidates from payors;
- obtaining market acceptance of our product candidates as viable treatment options;
- addressing any competing technological and market developments;
- receiving milestone and other payments under our current and any future collaboration arrangements;
- maintaining, protecting, expanding, and enforcing our portfolio of intellectual property rights;
- attracting, hiring, and retaining qualified personnel;
- general economic conditions, including conditions resulting from rising inflation and interest rates, recent bank failures and instability in the financial services sector, geopolitical uncertainty, and instability or war; and
- addressing any delays in our clinical trials or other impacts from the COVID-19 pandemic. a pandemic or other global health emergency.

Because of the numerous risks and uncertainties associated with drug development, we are unable to predict the timing or amount of our expenses, or when we will be able to generate any meaningful revenue or achieve or maintain profitability, if ever. In addition, our expenses could increase beyond our current expectations if we are required by the FDA, or foreign regulatory agencies, to perform studies in addition to those that we currently anticipate, or if there are any delays in any of our current or our future collaborators' clinical trials or the development of any of our product candidates. Even if one or more of our product candidates is approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved product candidate and ongoing compliance efforts.

Even if we are able to generate revenue from the sale of any approved products, we may not become profitable and may need to obtain additional funding to continue operations. Revenue from the sale of any product candidate for which regulatory approval is obtained will be dependent, in part, upon the size of the markets in the territories for which we gain regulatory approval, the accepted price for the product, the ability to get reimbursement at any price, and whether we own the commercial rights for that territory. If the number of addressable patients is not as significant as we anticipate, the indication approved by regulatory authorities is narrower than we expect, or the reasonably accepted population for treatment is narrowed by competition, physician choice choice. or treatment guidelines, we may not generate significant revenue from sales of such products, even if approved. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis.

Our failure to become and remain profitable would decrease the value of our company and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our pipeline of product candidates, or continue our operations and cause a decline in the value of our common stock, all or any of which may adversely affect our viability.

If we fail to obtain additional financing, we may be unable to complete the development and, if approved, commercialization of our product candidates.

Our operations have required substantial amounts of cash since inception. We currently fund our operations primarily with the proceeds from our follow-on offerings completed in January 2020 and October 2022, and payments received from our collaboration agreements with Biogen, Sanofi, and Takeda. Takeda, and a PIPE transaction completed in February 2024. We have a diversified portfolio with numerous programs at various stages of research, discovery, preclinical, and clinical development. Developing our product candidates is expensive, and we expect to continue to spend substantial amounts as we fund our early-stage research projects, and continue to advance our programs through preclinical and clinical development. Even if we are successful in developing our product candidates, obtaining regulatory approvals and launching and commercializing any product candidate will require substantial additional funding.

As of September 30, 2023 March 31, 2024, we had $1.12 $1.43 billion in cash, cash equivalents and marketable securities. We believe that our existing cash, cash equivalents and marketable securities will be sufficient to fund our projected operations through at least the next twelve months. Our estimate as to how long we expect our existing cash, cash equivalents, and marketable securities to be available to fund our operations is based on assumptions that may be proven inaccurate, and we could use our available capital resources sooner than we currently expect. Changing circumstances, some of which may be beyond our control, such as recent bank failures, geopolitical uncertainty, rising inflation or interest rates, or a perceived or actual economic downturn, may cause us to increase our spending significantly faster than we currently anticipate, and we may need to seek additional funds sooner than planned. We may also need to raise additional funds sooner than we anticipate if we choose to expand more rapidly than we presently anticipate.

We have no committed source of additional capital, and we cannot be certain that additional funding will be available when we need it, on terms acceptable to us or at all. We have no committed source of additional capital. If adequate capital is not available to us on a timely basis, we may be required to significantly delay, scale back, or discontinue our research and development programs or the commercialization of any product candidates, if approved, or be unable to continue or expand our operations or otherwise capitalize on our business opportunities, which could materially affect our business, financial condition, results of operations, and growth prospects and cause the price of our common stock to decline.

Due to the significant resources required for the development of our programs, and depending on our ability to access capital, we must prioritize development of certain product candidates. Moreover, we may expend our limited resources on programs that do not yield a successful product candidate and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

We have a diversified portfolio with numerous programs at various stages of research, discovery, preclinical, and clinical development. These programs require significant capital investment. We seek to maintain a process of prioritization and resource allocation to maintain an optimal balance between aggressively advancing lead programs and replenishing our portfolio. We regularly review the programs in our portfolio, and terminate those programs which do not meet our development criteria, which we have done a number of times in the past.

Due to the significant resources required for the development of our programs, we must focus our programs on specific diseases and disease pathways and decide which product candidates to pursue and advance and the amount of resources to allocate to each. Our decisions concerning the allocation of research, development, collaboration, management, and financial resources toward particular product candidates or therapeutic areas may not lead to the development of any viable commercial product and may divert resources away from better opportunities. Similarly, our potential decisions to delay, terminate, divest, or collaborate with third parties in respect of certain programs may subsequently also prove to be suboptimal and could cause us to miss valuable opportunities. If we make incorrect determinations regarding the viability or market potential of any of our programs or product candidates or misread trends in the biopharmaceutical industry, in particular for neurodegenerative and lysosomal storagediseases, our business, financial condition, results of operations, and growth prospects could be materially adversely affected. As a result, we may fail to capitalize on viable commercial products or profitable market opportunities, be required to forgo or delay pursuit of opportunities with other product candidates or other diseases and disease pathways that may later prove to have greater commercial potential than those we choose to pursue, or relinquish valuable rights to such product candidates through collaboration, licensing, or other royalty arrangements in cases in which it would have been advantageous for us to invest additional resources to retain sole development and commercialization rights.

A pandemic, epidemic or outbreak of an infectious disease, such as COVID-19, or the perception of its effects, may materially and adversely affect our business, operations, and financial condition.

Public health outbreaks, such as epidemics or pandemics, such as COVID-19, may significantly disrupt our business. Such outbreaks pose the risk that we or our employees, contractors, suppliers, and other partners may be prevented from conducting business activities for an indefinite period of time due to the spread of the disease, due to shutdowns that may be requested or mandated by federal, state, and local governmental authorities or certain employers, or due to the economic consequences associated with the pandemic. Business disruptions could include disruptions or restrictions on our ability to travel, as well as temporary closures of our facilities and the facilities of our partners, clinical trial sites, service providers, suppliers, or contract manufacturers. For example, the COVID-19 pandemic caused a temporary disruption in our ability to recruit participants for our clinical trials in the calendar year 2020 and the first quarter of 2021. While it is not possible to predict whether another pandemic, epidemic, or infectious disease outbreak similar to COVID-19 will materialize, any measures taken by governments and local authorities in response to such future health crises have the potential to disrupt and delay the initiation of new clinical trials, the progress of our ongoing clinical trials and our preclinical activities, and potentially the manufacture or shipment of both drug substance and finished drug product of our product candidates for preclinical testing and clinical trials, as well as adversely impact our business, financial condition, or operating results.

The continued impact of the COVID-19 pandemic may materially and adversely affect our business, operations and financial condition.

On May 11, 2023, the federal government ended the COVID-19 public health emergency, which ended a number of temporary changes made to federally funded programs, while some remain in effect. The full impact of the termination of the public health emergency on the FDA and other regulatory policies and operations remains unclear. In response to the COVID-19 pandemic, we implemented policies that enabled some of our employees to work remotely, which policies may continue for an indefinite period. Due to telecommuting patterns, modified work schedules, and enhanced safety protocols, our laboratory operations have at times and may again operate with decreased efficiency. Furthermore, our clinical trial sites for our clinical studies were impacted by the COVID-19 pandemic: in 2020, we experienced a pause in enrollment in our BIIB122/DNL151 Phase 1 and Phase 1b trials, our DNL343 Phase 1 and Phase 2/3 trials, and our ETV:IDS program observational biomarker study, and we have subsequently experienced certain delays in patient enrollment.

The FDA issued a number of COVID-19 related guidance documents for manufacturers and clinical trial sponsors in 2020 and 2021, many of which have expired or were withdrawn with the expiration of the COVID-19 public health emergency in May 2023, although some COVID-19 related guidance documents remain in effect. Should the FDA issue additional guidance that mandates material changes to our clinical trials in response to a pandemic or other public health outbreaks, the costs of such clinical trials may increase. To the extent we experience any ongoing pandemic disruptions or other public health emergencies, including a resurgence of COVID-19 cases, potential impacts to our business may include:

- include delays or difficulties in enrolling patients, in our clinical trials, particularly elderly subjects, who are at a higher risk of complications from COVID-19 or other public health outbreaks;
- difficulties interpreting data from our clinical trials due to the possible effects of COVID-19 or other public health outbreaks on subjects enrolled in our clinical trials;
- delays or difficulties in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff;

- diversion of healthcare resources away from the conduct of clinical trials, including the diversion of hospitals serving as our clinical impacted by trial sites and hospital staff supporting clinical trials;
- interruption of key clinical trial activities, such as clinical trial site monitoring, due to limitations on travel imposed or recommended by federal or state governments, employers and others;
- delays in receiving approval from local regulatory authorities to initiate our planned clinical trials;
- interruption of, or delays in receiving, supplies of our product candidates from our contract manufacturing organizations due to disruptions, supply chain issues, staffing shortages, production slowdowns or stoppages;
- delays or difficulties in furthering our preclinical and clinical programs, due disruptions to interruptions or limitations in our third party service providers' business operations;
- interruption in global shipping that has affected the transport of clinical trial materials, such as investigational drug products used in our clinical trials;
- changes in clinical trial site procedures and requirements as well as regulatory requirements for conducting clinical trials during a pandemic or other public health emergency;
- delays or interruptions in the operations of or necessary interactions with the FDA or other regulators; and
- limitations our service providers, any of which could have a material adverse effect on employee resources that would otherwise be focused on the conduct of our nonclinical studies business and clinical trials, either because of sickness of employees and their families or the desire of employees to avoid contact with large groups of people.development plans.

To the extent another pandemic or other public health outbreak adversely affects our business, operations and financial condition in the future, it may also have the effect of heightening many of the risks described in this "Risk Factors" section.

Risks Related to the Discovery, Development, and Commercialization of Our Product Candidates

Research and development of biopharmaceutical products is inherently risky. We are heavily dependent on the successful development of our BBB platform technology and the programs currently in our pipeline, which are in preclinical and clinical development stages. We cannot give any assurance that any of our product candidates will receive regulatory, including marketing, approval, which is necessary before they can be commercialized.

We are at an early stage of development of many of the product candidates currently in our programs and are further developing our BBB platform technology. To date, we have invested substantially all of our efforts and financial resources to identify, acquire intellectual property for, and develop our BBB platform technology and our programs, including conducting preclinical studies and clinical trials, and providing general and administrative support for these operations. Our future success is dependent on our ability to successfully develop, obtain regulatory approval for, and then successfully commercialize our product candidates, and we may fail to do so for many reasons, including the following:

- our product candidates may not successfully complete preclinical studies or clinical trials;
- our drug delivery platform technology may not be clinically viable;
- a product candidate 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;
- our competitors may develop therapeutics that render our product candidates obsolete or less attractive;
- our competitors may develop platform technologies to deliver large molecule therapeutics across the BBB that render our platform technology obsolete or less attractive;
- the product candidates and BBB platform technology that we develop may not be sufficiently covered by intellectual property for which we hold exclusive rights;
- the product candidates and BBB platform technology that we develop may be covered by third parties' patents or other intellectual property or exclusive rights;
- the market for a product candidate may change so that the continued development of that product candidate is no longer reasonable or commercially attractive;

- a product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all;

- if a product candidate obtains regulatory approval, we may be unable to establish sales and marketing capabilities, or successfully market such approved product candidate; and

- a product candidate may not be accepted as safe and effective by patients, the medical community or third-party payors, if applicable.

If any of these events occur, we may be forced to abandon our development efforts for a program or programs, which would could have a material adverse effect on our business.

We may not be successful in our efforts to further develop our BBB platform technology and current product candidates. We are not permitted to market or promote any of our product candidates before we receive regulatory approval from the FDA or comparable foreign regulatory authorities, and we may never receive such regulatory approval for any of our product candidates. Our product candidates are in the early stages of development and will require significant additional clinical development, management of preclinical, clinical, and manufacturing activities, regulatory approval, adequate manufacturing supply, a commercial organization, and significant marketing efforts before we generate any revenue from product sales, if at all.

We have never completed a clinical development program. We have previously discontinued the development of certain molecules prior to completion of preclinical development because we did not believe they met our criteria for potential clinical success. Further, we cannot be certain that any of our product candidates will be successful in clinical trials. For instance, in August 2023, together with our collaboration partner Takeda, we discontinued development of TAK-920/DNL919 (ATV:TREM2) in Alzheimer's disease, based on data from the Phase 1 study and the rapidly evolving treatment landscape and shifted our efforts to exploring back-up molecules. We may in the future advance product candidates into clinical trials and terminate such trials prior to their completion.

If any of our product candidates successfully complete clinical trials, we generally plan to seek regulatory approval to market our product candidates in the United States, the European Union ("EU"), and in additional foreign countries where we believe there is a viable commercial opportunity. We have never commenced, compiled, or submitted an application seeking regulatory approval to market any product candidate, and may never receive such regulatory approval even if a product candidate successfully completes clinical trials, which would adversely affect our viability. To obtain regulatory approval in countries outside the United States, we must comply with numerous and varying regulatory requirements of such other countries regarding safety, efficacy or potency, purity, chemistry, manufacturing and controls, clinical trials, commercial sales, pricing, and distribution of our product candidates. We may also rely on our collaborators or partners to conduct the required activities to support an application for regulatory approval, and to seek approval, for one or more of our product candidates. We cannot be sure that our collaborators or partners will conduct these activities or do so within the time frame we desire. Even if we (or our collaborators or partners) are successful in obtaining approval in one jurisdiction, we cannot ensure that we will obtain approval in any other jurisdictions. If we are unable to obtain approval for our product candidates in multiple jurisdictions, our revenue, business, financial condition, results of operations and growth prospects could be negatively affected.

Even if we receive regulatory approval to market any of our product candidates, whether for the treatment of neurodegenerative and lysosomal storagediseases or other diseases, we cannot assure you that any such product candidate will be successfully commercialized, widely accepted in the marketplace or more effective than other commercially available alternatives.

Investment in biopharmaceutical product development involves significant risk that any product candidate will fail to demonstrate adequate efficacy or potency, or an acceptable safety profile, gain regulatory approval, and become commercially viable. We cannot provide any assurance that we will be able to successfully advance any of our product candidates through the development process or, if approved, successfully commercialize any of our product candidates.

We may not be successful in our efforts to continue to create a pipeline of product candidates or to develop commercially successful products. If we fail to successfully identify and develop additional product candidates, our commercial opportunity may be limited.

One of our strategies is to identify and pursue clinical development of additional product candidates. We currently have several programs in the research, discovery and preclinical stages of development. Identifying, developing, obtaining regulatory approval for, and commercializing additional product candidates for the treatment of neurodegenerative and lysosomal storage diseases will require substantial additional funding and is prone to the risks of failure inherent in drug development. We cannot provide

you any assurance that we will be able to successfully identify or acquire additional product candidates, advance any of these additional product candidates through the development process, successfully commercialize any such additional product candidates, if approved, or assemble sufficient resources to identify, acquire, develop or, if approved, commercialize additional product candidates. If we are unable to successfully identify, acquire, develop, and commercialize additional product candidates, our commercial opportunity may be limited.

We have concentrated a substantial portion of our research and development efforts on the treatment of neurodegenerative and lysosomal storage diseases, a field fields that has have seen limited success in drug development. Further, our product candidates are based on new approaches and novel technology, which makes it difficult to predict the time and cost of product candidate development and subsequently obtaining regulatory approval.

We have focused our research and development efforts on addressing neurodegenerative diseases. and lysosomal storage diseases. Collectively, efforts by biopharmaceutical companies in the field fields of neurodegenerative and lysosomal storage diseases have seen limited success in drug development. There are few effective therapeutic options available for patients with neurodegenerative diseases, such as Alzheimer's disease, Parkinson's disease, and ALS, and other neurodegenerative diseases. lysosomal storage diseases, such as Hunter syndrome and Sanfilippo syndrome. Our future success is highly dependent on the successful development of our BBB platform technology and our product candidates for treating neurodegenerative diseases. and lysosomal storage diseases. Developing and, if approved, commercializing our product candidates for treatment of neurodegenerative and lysosomal storagediseases subjects us to a number of challenges, including engineering product candidates to cross the BBB to enable optimal concentration of the therapeutic in the brain and obtaining regulatory approval from the FDA and other regulatory authorities who have only a limited set of precedents to rely on.

Our approach to the treatment of neurodegenerative and lysosomal storagediseases aims to identify and select targets with a genetic link to neurodegenerative and lysosomal storagediseases, as applicable, identify and develop molecules that engage the intended target, identify and develop biomarkers, which are biological molecules found in blood, other bodily fluids or tissues that are signs of a normal or abnormal process or of a condition or disease, to select the right patient population and demonstrate target engagement, pathway engagement and impact on disease progression of our molecules, and engineer our molecules to cross the BBB and act directly in the brain. This strategy may not prove to be successful. We may not be able to discover, develop, and utilize biomarkers to demonstrate target engagement, pathway engagement, and the impact on disease progression of our molecules. We cannot be sure that our approach will yield satisfactory therapeutic products that are safe and effective, scalable, or profitable. Moreover, public perception of drug safety issues, including adoption of new therapeutics or novel approaches to treatment, may adversely influence the willingness of subjects to participate in clinical trials, or if approved, of physicians to subscribe to novel treatments.

We may encounter substantial delays in our clinical trials, or may not be able to conduct or complete our clinical trials on the timelines we expect, if at all.

Clinical testing is expensive, time consuming, and subject to uncertainty. We cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, if at all. We cannot be sure that submission of an investigational new drug application ("IND"), or a clinical trial application ("CTA"), will result in the FDA or EMA, as applicable, allowing clinical trials to begin in a timely manner, if at all. Moreover, even if these trials begin, issues may arise that could suspend or terminate such clinical trials. A failure of one or more clinical trials can occur at any stage of testing, and our future clinical trials may not be successful. Events that may prevent successful or timely initiation or completion of clinical trials include:

- inability to generate sufficient preclinical, toxicology, or other *in vivo* or *in vitro* data to support the initiation or continuation of clinical trials;
- delays in confirming target engagement, patient selection, or other relevant biomarkers to be utilized in preclinical and clinical product candidate development;
- delays in reaching a consensus with regulatory agencies on trial design;
- delays in reaching agreement on acceptable terms with prospective CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and clinical trial sites;
- delays in identifying, recruiting, and training suitable clinical investigators;
- delays in obtaining required Institutional Review Board ("IRB") approval at each clinical trial site;
- imposition of a temporary or permanent clinical hold by regulatory agencies for a number of reasons, including after review of an IND or amendment, CTA or amendment, or equivalent application or amendment; as a result of a new safety finding that presents unreasonable risk to clinical trial participants; a negative finding from an inspection of our clinical trial operations or trial sites; developments on trials conducted by competitors for related technology that raises FDA or EMA concerns about risk to patients of the technology broadly; or if the FDA or EMA finds that the investigational protocol or plan is clearly deficient to meet its stated objectives;

- delays in identifying, recruiting, and enrolling suitable patients to participate in our clinical trials, and delays caused by patients withdrawing from clinical trials or failing to return for post-treatment follow-up;
- difficulty collaborating with patient groups and investigators;
- failure by our CROs, other third parties, or us to adhere to clinical trial requirements;
- failure to perform in accordance with the FDA's or any other regulatory authority's current good clinical practices ("cGCPs") requirements, or other regulatory guidelines in other countries;
- occurrence of adverse events associated with the product candidate that are viewed to outweigh its potential benefits;
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols;
- changes in the approval policies or regulations of the FDA or other regulatory authorities;
- changes in the standard of care on which a clinical development plan was based, which may require new or additional trials;
- the cost of clinical trials of our product candidates being greater than we anticipate;
- clinical trials of our product candidates producing negative or inconclusive results, which may result in us or our collaborators deciding, or regulators requiring us, to conduct additional clinical trials or abandon product development programs;
- transfer of manufacturing processes from our academic collaborators to larger-scale facilities operated by a CDMO or by us, and delays or failure by our CDMOs or us to make any necessary changes to such manufacturing process;
- delays in manufacturing, testing, releasing, validating, or importing/exporting sufficient stable quantities of our product candidates for use in clinical trials or the inability to do any of the foregoing; and
- delays associated with a pandemic or other public health emergency.

Any inability to successfully initiate or complete clinical trials could result in additional costs to us or impair our ability to generate revenue. In addition, if we make manufacturing or formulation changes to our product candidates, we or our collaborators may be required to or we may elect to conduct additional studies to bridge our modified product candidates to earlier versions. Clinical trial delays could also shorten any periods during which our products have patent protection and may allow our competitors to bring products to market before we do, which could impair our ability to successfully commercialize our product candidates and may harm our business and results of operations.

We could also encounter delays if a clinical trial is suspended or terminated by us or our collaborators, by the data safety monitoring board for such trial, or by any regulatory authority, or if the IRBs of the institutions in which such trials are being conducted suspend or terminate the participation of their clinical investigators and sites subject to their review. Such authorities may suspend or terminate a clinical trial due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA, EMA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a product candidate, changes in governmental regulations or administrative actions, or lack of adequate funding to continue the clinical trial.

For example, in January 2022, we announced that the TAK-920/DNL919 (ATV:TREM2) IND application had been placed on clinical hold by the FDA. In August 2023 we announced that, in agreement with Takeda, we would discontinue clinical development of TAK-920/DNL919 in Alzheimer's disease. We cannot assure you that we will ever resume the clinical program for TAK-920/DNL919, nor can we assure you that our other product candidates will not be subject to new, partial or full clinical holds in the future, which may impact development plans.

Refer to "Item 1. Business—Our Programs" of Form 10-K for a more detailed discussion of adverse effects ("AEs") and significant adverse effects ("SAEs") observed in We or our reported clinical trials for BIIB122/DNL151 and DNL310.

We collaborators may in the future advance product candidates into clinical trials and terminate such trials prior to their completion, which could adversely affect our business. Further, after the commencement of clinical trials, we or our collaborators may discontinue advancement of lead molecules, such as the TAK-920/DNL919 program, or pause the advancement of lead molecules in favor of a backup molecule with a superior safety or efficacy profile, such as we did in our RIPK1 program, switching our focus from DNL747 to SAR443820/DNL788.

Delays in the completion of any clinical trial of our product candidates will increase our costs, slow down our product candidate development and approval process and delay or potentially jeopardize our ability to commence product sales and generate revenue. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates.

We may encounter difficulties enrolling and/or retaining patients in our clinical trials, and our clinical development activities could thereby be delayed or otherwise adversely affected.

The timely completion of clinical trials in accordance with their protocols depends, among other things, on our ability to enroll a sufficient number of patients who remain in the trial until its conclusion. We may experience difficulties in patient enrollment and retention in our clinical trials for a variety of reasons, including:

- public health crises, such as the COVID-19 pandemic;
- the size and nature of the patient population;
- the patient eligibility criteria defined in the protocol, including biomarker-driven identification and/or certain highly-specific criteria related to stage of disease progression, which may limit the patient populations eligible for our clinical trials to a greater extent than competing clinical trials for the same indication that do not have biomarker-driven patient eligibility criteria;
- the size of the study population required for analysis of the trial's primary endpoints;
- the proximity of patients to a trial site;
- the design of the trial;
- our ability to recruit clinical trial investigators with the appropriate competencies and experience;
- competing clinical trials for similar therapies or targeting patient populations meeting our patient eligibility criteria;
- clinicians' and patients' perceptions as to the potential advantages and side effects of the product candidate being studied in relation to other available therapies and product candidates;
- our ability to obtain and maintain patient consents; and
- the risk that patients enrolled in clinical trials will not complete such trials, for any reason, including the risk of higher drop-out rates if participants become infected with the COVID-19 virus or other infectious diseases that impact their participation in our trials.

Our inability to enroll and retain a sufficient number of patients for our clinical trials would result in significant delays or may require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may result in increased development costs for our product candidates and jeopardize our ability to obtain marketing approval for the sale of our product candidates. Furthermore, even if we are able to enroll a sufficient number of patients for our clinical trials, we may have difficulty maintaining participation in our clinical trials through the treatment and any follow-up periods, which could delay or negatively impact the anticipated readouts from our clinical trials, delay our regulatory submissions, and increase the costs of the clinical trials.

Our clinical trials may reveal significant adverse events, toxicities, or other side effects and may fail to demonstrate substantial evidence of the safety and efficacy or potency of our product candidates, which would prevent, delay, or limit the scope of regulatory approval and commercialization.

Before obtaining regulatory approvals for the commercial sale of any of our product candidates, we must demonstrate through lengthy, complex, and expensive preclinical studies and clinical trials that our product candidates are both safe and effective for use in each target indication. For those product candidates that are subject to regulation as biological drug products, we will need to demonstrate that they are safe, pure, and potent for use in their target indications. Each product candidate must demonstrate an adequate risk versus benefit profile in its intended patient population and for its intended use.

Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. The results of preclinical studies of our product candidates may not be predictive of the results of early-stage or later-stage clinical trials, and results of early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials. The results of clinical trials in one set of patients or disease indications may not be predictive of those obtained in another. In some instances, there can be significant variability in safety or efficacy or potency results between different clinical trials of the same product candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, changes in and adherence to the dosing regimen and other clinical trial protocols and the rate of dropout among clinical trial participants. Open-label extension studies may also extend the timing and increase the cost of clinical development substantially. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy or potency profile despite having progressed through preclinical studies and initial clinical trials. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or potency or unacceptable safety issues, notwithstanding promising results in earlier trials. This is particularly true in neurodegenerative diseases and lysosomal storage diseases, where failure rates historically have been higher than in many other disease areas. Most product candidates that begin clinical trials are never approved by regulatory authorities for commercialization.

We cannot be certain that our current clinical trials or any other future clinical trials will be successful. Additionally, any safety concerns observed in any one of our clinical trials in our targeted indications could limit the prospects for regulatory approval of our product candidates in those and other indications, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

Even if such clinical trials are successfully completed, we cannot guarantee that the FDA will approve the product candidates for the proposed indications, and more trials could be required before we submit our product candidates for approval. To the extent that the results of the trials are not satisfactory to the FDA or foreign regulatory authorities for support of a marketing application, we may be required to expend significant resources, which may not be available to us, or to conduct additional trials in support of potential approval of our product candidates. Even if regulatory approval is secured for any of our product candidates, the terms of such approval, such as requiring us to narrow our indications to a smaller subset, may also limit its commercial potential.

Interim, topline, and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available, and are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publicly disclose preliminary, interim, or topline data from our nonclinical studies and clinical trials, which are based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations, and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the topline results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Topline data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, preliminary, interim, or topline data should be viewed with caution until the final data are available. In addition, we may report interim analyses of only certain endpoints rather than all endpoints. Adverse changes between interim data and final data could significantly harm our business and prospects. Further, additional disclosure of interim data by us or by our competitors in the future could result in volatility in the price of our common stock.

Further, others, including our collaborators or regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions, or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approval or commercialization of the particular product candidate and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is typically selected from a more extensive amount of available information. You or others may not agree with what we determine is the material or otherwise appropriate information to include in our disclosure, and any information we determine not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities or otherwise regarding a particular product candidate or our business. If the preliminary or topline data that we report differ from late, final, or actual results, or if others, including our collaborators or regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize our product candidates may be harmed.

We face significant competition in an environment of rapid technological and scientific change, and our operating results may suffer if we fail to compete effectively.

The development and commercialization of new drug products is highly competitive. Moreover, the neurodegenerative field is and lysosomal storage ("LS") fields are characterized by strong and increasing competition. Our potential competitors include pharmaceutical companies, biotechnology companies, academic institutions, government agencies, and other public and private research organizations that conduct research. Our competitors, either alone or with collaborative partners, may succeed in developing, acquiring, or licensing on an exclusive basis drug or biologic products that are more effective, safer, more easily commercialized, or less costly than our product candidates or may develop proprietary technologies or secure patent protection that we may need for the development of our technologies and products.

A number of large pharmaceutical and biotechnology companies are developing products for the treatment of the neurodegenerative and lysosomal storage disease indications for which we have research programs, including Alzheimer's disease, Parkinson's disease, Hunter syndrome, and ALS. Companies that we are aware are developing therapeutics in the neurodegenerative and lysosomal storage disease area areas include companies with significant financial resources, such as Abbvie, Alector, AstraZeneca, Biogen, Bristol-Myers Squibb, Eli Lilly (including Prevail Therapeutics, its wholly owned subsidiary), GlaxoSmithKline, Ionis, JCR Pharmaceuticals, Johnson & Johnson, Novartis,

Roche (including Genentech, its wholly owned subsidiary), Sanofi and Takeda. resources. In addition to competition from other companies targeting neurodegenerative indications, any products we may develop may also face competition from other types of therapies, such as gene-editing therapies.

Many of our current or potential competitors have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals, and marketing approved products than we do. Mergers and acquisitions may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. Our competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient, or are less expensive than any products that we may develop. Furthermore, currently approved products could be discovered to have application for treatment of neurodegenerative or lysosomal storage disease indications, which could give such products significant regulatory and market timing advantages over any of our product candidates. Our competitors also may obtain regulatory approval for their products more rapidly than we do, and may obtain orphan product exclusivity for indications our product candidates are targeting, which could result in our competitors establishing a strong market position before we are able to enter the market. Additionally, products or technologies developed by our competitors may render our potential product candidates uneconomical or obsolete, and we may not be successful in marketing any product candidates we may develop against competitors.

The manufacture of our product candidates, particularly those that utilize our BBB platform technology, is complex and we may encounter difficulties in production. We may fail to successfully manufacture our product candidates, operate our own manufacturing facility, or obtain regulatory approval to utilize or commercialize from our manufacturing facility, which could adversely affect our clinical trials and the commercial viability of our product candidates.

The processes involved in manufacturing our drug and biological product candidates, particularly those that utilize our BBB platform technology, are complex, expensive, highly regulated and subject to multiple risks. Additionally, the manufacture of biologics involves complex processes, including developing cells or cell systems to produce the biologic, growing large quantities of such cells, and harvesting and purifying the biologic produced by them. As a result, the cost to manufacture a biologic is generally far higher than traditional small molecule chemical compounds, and the biologics manufacturing process is less reliable and is difficult to reproduce. Manufacturing biologics is highly susceptible to product loss due to contamination, equipment failure, improper installation or operation of equipment, vendor or operator error, inconsistency in yields, variability in product characteristics, and difficulties in scaling the production process. Even minor deviations from normal manufacturing processes could result in reduced production yields, product defects, and other supply disruptions. Further, as product candidates are developed through preclinical studies to late-stage clinical trials towards approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods, are altered along the way in an effort to optimize processes and results. Such changes carry the risk that they will not achieve these intended objectives, and any of these changes could cause our product candidates to perform differently and affect the results of planned clinical trials or other future clinical trials.

In order to conduct clinical trials of our product candidates, or supply commercial products, if approved, we will need to manufacture them in small and large quantities. Our manufacturing partners may be unable to successfully increase the manufacturing capacity for any of our product candidates in a timely or cost-effective manner, or at all. In addition, quality issues may arise during scale-up activities. If our manufacturing partners are unable to successfully scale up the manufacture of our product candidates in sufficient quality and quantity, the development, testing, and clinical trials of that product candidate may be delayed or become infeasible, and regulatory approval or commercial launch of any resulting product may be delayed or not obtained, which could significantly harm our business. The same risks would apply to our internal manufacturing facilities and capabilities, which we are actively building in Salt Lake City, Utah. Under an operating lease for approximately 60,000 rentable square feet of laboratory, office, and warehouse premises, we have initiated the build-out of our Utah site to expand our clinical manufacturing capabilities for biologic therapeutics including the manufacture of materials for toxicology studies and drug substance for early human clinical studies. In addition, building internal manufacturing capacity carries significant risks in terms of being able to plan, design, and execute on a complex project to build manufacturing facilities in a timely and cost-efficient manner. To date, we have experienced delays with the manufacturing site build-out, and there can be no assurance that our current and future efforts to scale our internal manufacturing capabilities will succeed.

In addition, the manufacturing process, including any material modifications in the manufacturing process for any products that we may develop, is subject to regulatory authority approval processes and continuous oversight, and we will need to contract with manufacturers who can meet all applicable regulatory authority requirements, including complying with current good manufacturing practices ("cGMPs"), on an ongoing basis. If we or our third-party manufacturers are unable to reliably produce products to specifications acceptable to regulatory authorities, we may not obtain or maintain the approvals we need to commercialize such products. Even if we obtain regulatory approval for any of our product candidates, there is no assurance that either we or our CDMOs will be able to manufacture the approved product to specifications acceptable to the regulatory authorities, to produce it in sufficient quantities to meet the requirements for the potential launch of the product, or to meet potential future demand. Any of these challenges could delay completion of clinical trials, require bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay approval of our product candidate, impair commercialization efforts, increase our cost of goods, and have an adverse effect on our business, financial condition, results of operations and growth prospects.

If, in the future, we are unable to establish sales and marketing capabilities or enter into agreements with third parties to sell and market any product candidates we may develop, we may not be successful in commercializing those product candidates if and when they are approved.

We do not have a sales or marketing infrastructure and have no experience in the sale, marketing, or distribution of pharmaceutical products. To achieve commercial success for any approved product for which we retain sales and marketing responsibilities, we must either develop a sales and marketing organization or outsource these functions to third parties. In the future, we may choose to build a focused sales, marketing, and commercial support infrastructure to sell, or participate in sales activities with our collaborators for, some of our product candidates if and when they are approved.

There are risks involved with both establishing our own commercial capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force or reimbursement specialists is expensive and time consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing and other commercialization capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our commercialization personnel.

Factors that may inhibit our efforts to commercialize any approved product on our own include:

- our inability to recruit and retain adequate numbers of effective sales, marketing, reimbursement, customer service, medical affairs, and other support personnel;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future approved products;
- the inability of reimbursement professionals to negotiate arrangements for formulary access, reimbursement, and other acceptance by payors;
- the inability to price our products at a sufficient price point to ensure an adequate and attractive level of profitability;
- restricted or closed distribution channels that make it difficult to distribute our products to segments of the patient population;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent commercialization organization.

If we enter into arrangements with third parties to perform sales, marketing, commercial support, and distribution services, our product revenue or the profitability of product revenue may be lower than if we were to market and sell any products we may develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to commercialize our product candidates or may be unable to do so on terms that are favorable to us. We may have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively. If we do not establish commercialization capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates if approved.

Even if any product candidates we develop receive marketing approval, they may fail to achieve the degree of market acceptance by physicians, patients, healthcare payors, and others in the medical community necessary for commercial success.

The commercial success of any of our product candidates will depend upon its degree of market acceptance by physicians, patients, third-party payors, and others in the medical community. Even if any product candidates we may develop receive marketing approval, they may nonetheless fail to gain sufficient market acceptance by physicians, patients, healthcare payors, and others in the medical community. The degree of market acceptance of any product candidates we may develop, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy or potency and safety of such product candidates as demonstrated in pivotal clinical trials and published in peer-reviewed journals;
- the potential and perceived advantages compared to alternative treatments;
- the ability to offer our products for sale at competitive prices;

- the ability to offer appropriate patient access programs, such as co-pay assistance;
- the extent to which physicians recommend our products to their patients;
- convenience and ease of dosing and administration compared to alternative treatments;
- the clinical indications for which the product candidate is approved by FDA, EMA or other regulatory agencies;

- product labeling or product insert requirements of the FDA, EMA or other comparable foreign regulatory authorities, including any limitations, contraindications or warnings contained in a product's approved labeling;
- restrictions on how the product is distributed;
- the timing of market introduction of competitive products;
- publicity concerning our products or competing products and treatments;
- the strength of marketing and distribution support;
- sufficient third-party coverage or reimbursement; and
- the prevalence and severity of any side effects.

If any product candidates we develop do not achieve an adequate level of acceptance, we may not generate significant product revenue, and we may not become profitable.

Even if we are able to commercialize any product candidates, such products may become subject to unfavorable pricing regulations, third-party reimbursement practices, or healthcare reform initiatives, which would harm our business.

The regulations that govern marketing approvals, pricing, and reimbursement for new drugs vary widely from country to country. In the United States, legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenue we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if any product candidates we may develop obtain marketing approval.

Our ability to successfully commercialize any products that we may develop also will depend in part on the extent to which reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers, and other organizations. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Government authorities currently impose mandatory discounts for certain patient groups, such as Medicare, Medicaid and Veterans Affairs ("VA"), hospitals, and may seek to increase such discounts at any time. Future regulation may negatively impact the price of our products, if approved. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot be sure that reimbursement will be available for any product candidate that we commercialize and, if reimbursement is available, the level of reimbursement. Reimbursement may impact the demand for, or the price of, any product candidate for which we obtain marketing approval. In order to get reimbursement, physicians may need to show that patients have superior treatment outcomes with our products compared to standard of care drugs, including lower-priced generic versions of standard of care drugs. If reimbursement is not available or is available only to limited levels, we may not be able to successfully commercialize any product candidate for which we obtain marketing approval. In the United States, no uniform policy of coverage and reimbursement for products exists among third-party payors and coverage and reimbursement levels for products can differ significantly from payor to payor. As a result, the coverage determination process is often a time consuming and costly process that may require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance.

There may be significant delays in obtaining reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the medicine is approved by regulatory authorities. Moreover, eligibility for reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale, and distribution. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies. Our inability to promptly obtain coverage and profitable payment rates from both government-funded and private payors for any approved products we may develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize product candidates, and our overall financial condition.

If any of our small molecule product candidates obtain regulatory approval, additional competitors could enter the market with generic versions of such drugs, which may result in a material decline in sales of affected products.

Under the Drug Price Competition and Patent Term Restoration Act of 1984 (the "Hatch-Waxman Act"), a pharmaceutical manufacturer may file an abbreviated new drug application ("ANDA") seeking approval of a generic copy of an approved, small molecule innovator product. Under the Hatch-Waxman Act, a manufacturer may also submit a new drug application ("NDA") under section 505(b)(2) that references the FDA's prior approval of the small molecule innovator product. A 505(b)(2) NDA product may be for a new or improved version of the original innovator product. The Hatch-Waxman Act also provides for certain periods of regulatory exclusivity, which preclude FDA approval (or in some circumstances, FDA filing and reviewing) of an ANDA or 505(b)(2) NDA. These include, subject to certain exceptions, the period during which an FDA-approved drug is subject to orphan drug exclusivity. In addition to the benefits of regulatory exclusivity, an innovator NDA holder may have patents claiming the active ingredient, product formulation or an approved use of the drug, which would be listed with the product in the FDA publication, “Approved Drug Products with Therapeutic Equivalence Evaluations,” known as the “Orange Book.” If there are patents listed in the Orange Book, a generic or 505(b)(2) applicant that seeks to market its product before expiration of the patents must include in the ANDA a “Paragraph IV certification,” challenging the validity or enforceability of, or claiming non-infringement of, the listed patent or patents. Notice of the certification must be given to the innovator, too, and if within 45 days of receiving notice the innovator sues to protect its patents, approval of the ANDA is stayed for 30 months, or as lengthened or shortened by the court.

Accordingly, if any of our small molecule product candidates are approved, competitors could file ANDAs for generic versions of our small molecule drug products or 505(b)(2) NDAs that reference our small molecule drug products, respectively. If there are patents listed for our small molecule drug products in the Orange Book, those ANDAs and 505(b)(2) NDAs would be required to include a certification as to each listed patent indicating whether the ANDA applicant does or does not intend to challenge the patent. We cannot predict which, if any, patents in our current portfolio or patents we may obtain in the future will be eligible for listing in the Orange Book, how any generic competitor would address such patents, whether we would sue on any such patents, or the outcome of any such suit.

We may not be successful in securing or maintaining proprietary patent protection for products and technologies we develop or license. Moreover, if any of our owned or in-licensed patents that are listed in the Orange Book are successfully challenged by way of a Paragraph IV certification and subsequent litigation, the affected product could immediately face generic competition and its sales would likely decline rapidly and materially. Should sales decline, we may have to write off a portion or all of the intangible assets associated with the affected product and our results of operations and cash flows could be materially and adversely affected. See “Risks Related to Our Intellectual Property.”

Our biologic, or large molecule, product candidates for which we intend to seek approval may face competition sooner than anticipated.

Even if we are successful in achieving regulatory approval to commercialize a product candidate faster than our competitors, our large molecule product candidates may face competition from biosimilar products. In the United States, our large molecule product candidates are regulated by the FDA as biologic products and we intend to seek approval for these product candidates pursuant to the biologics license application ("BLA"), pathway. The Biologics Price Competition and Innovation Act of 2009 (the "BPCIA"), created an abbreviated pathway for the approval of biosimilar and interchangeable biologic products. The abbreviated regulatory pathway establishes legal authority for the FDA to review and approve biosimilar biologics, including the possible designation of a biosimilar as “interchangeable” based on its similarity to an existing brand product. Under the BPCIA, an application for a biosimilar product cannot be approved by the FDA until 12 years after the original branded product was approved under a BLA. The law is complex and is still being interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and meaning are subject to uncertainty. While it is uncertain when such processes intended to implement BPCIA may be fully adopted by the FDA, any such processes could have a material adverse effect on the future commercial prospects for our large molecule product candidates.

We believe that any of our large molecule product candidates approved as a biologic product under a BLA should qualify for the 12-year period of exclusivity. However, there is a risk that this exclusivity could be shortened due to congressional action or otherwise, or that the FDA will not consider our product candidates to be reference products for competing products, potentially creating the opportunity for generic competition sooner than anticipated. Moreover, the extent to which a biosimilar product, once approved, will be substituted for any one of our reference products in a way that is similar to traditional generic substitution for non-biologic products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing. In addition, a competitor could decide to forego the biosimilar approval path and submit a full BLA after completing its own preclinical studies and clinical trials. In such cases, any exclusivity to which we may be eligible under the BPCIA would not prevent the competitor from marketing its product as soon as it is approved.

In Europe, if competitors are able to obtain marketing approval for biosimilars referencing our large molecule product candidates, such products may become subject to competition from such biosimilars, with the attendant competitive pressure and potential adverse consequences. Such competitive products may be able to immediately compete with us in each indication for which our product candidates may have received approval.

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of our product candidates.

We face an inherent risk of product liability as a result of the clinical testing of our product candidates and will face an even greater risk when and if we commercialize any products. For example, we may be sued if our product candidates cause or are perceived to cause injury or are found to be otherwise unsuitable during clinical testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability or a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit testing and commercialization of our product candidates. Even successful defense would require significant costs to defend litigation and a diversion of management's time and resources. Regardless of the merits or eventual outcome, liability claims may result in a decreased or interrupted demand for our products, injury to our reputation, withdrawal of clinical trial participants and inability to continue clinical trials, and initiation of investigation by regulators. Any successful liability claims could result in substantial monetary awards to trial participants or patients; product recalls, withdrawals, or labeling, marketing or promotional restrictions; loss of revenue; exhaustion of any available insurance and our capital resources; the inability to commercialize any product candidate; and a decline in our share price.

Our inability to obtain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of products we develop, alone or with collaborators. Our insurance policies may have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We may have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts. Even if our agreements with any future corporate collaborators entitle us to indemnification against losses, such indemnification may not be available or adequate should any claim arise.

Risks Related to Regulatory Approval and Other Legal Compliance Matters

The regulatory approval processes of the FDA, EMA, and comparable foreign regulatory authorities are lengthy, time consuming, and inherently unpredictable. If we are ultimately unable to obtain regulatory approval for our product candidates, we will be unable to generate product revenue and our business will be substantially harmed.

The time required to obtain approval by the FDA, EMA, and comparable foreign regulatory authorities is unpredictable, typically takes many years following the commencement of clinical trials, and depends upon numerous factors, including the type, complexity and novelty of the product candidates involved. In addition, approval policies, regulations, or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions, which may cause delays in the approval or the decision not to approve an application. For example, if the Supreme Court reverses or curtails the *Chevron* doctrine, which gives deference to regulatory agencies in litigation against the FDA and other agencies, more companies may bring lawsuits against the FDA to challenge longstanding decisions and policies of the FDA, which could undermine the FDA's authority, lead to uncertainties in the industry, and disrupt the FDA's normal operations, which could delay the FDA's review of our marketing applications.

Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other studies. Moreover, regulatory authorities may fail to approve companion diagnostics that we contemplate using with our therapeutic product candidates. We have not submitted for, or obtained regulatory approval for any product candidate, and it is possible that none of our existing product candidates or any product candidates we may seek to develop in the future will ever obtain regulatory approval.

Applications for our product candidates could fail to receive regulatory approval in an initial or subsequent indication for many reasons, including but not limited to the following:

- regulatory authorities may disagree with the design, implementation, or results of our clinical trials;

- regulatory authorities may determine that our product candidates are not safe and effective, only moderately effective, or have undesirable or unintended side effects, toxicities, or other characteristics that preclude our obtaining marketing approval or prevent or limit commercial use;
- the population studied in the clinical program may not be sufficiently broad or representative to assure efficacy or potency and safety in the full population for which we seek approval;
- we may be unable to demonstrate to the regulatory authorities that a product candidate's risk-benefit ratio when compared to the standard of care is acceptable;
- regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- the data collected from clinical trials of our product candidates may not be sufficient to support the submission of an NDA, BLA, or other submission or to obtain regulatory approval in the United States or elsewhere;
- we may be unable to demonstrate to the regulatory authorities that a product candidate's risk-benefit ratio for its proposed indication is acceptable;
- regulatory authorities may fail to approve the manufacturing processes, test procedures and specifications, or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; and
- the approval policies or regulations of the regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

This lengthy approval process, as well as the unpredictability of the results of clinical trials, may result in our failing to obtain regulatory approval to market any of our product candidates, which would significantly harm our business, results of operations, and prospects.

Our product candidates may cause undesirable side effects or have other properties that could halt their clinical development, prevent their regulatory approval, limit their commercial potential, or result in significant negative consequences.

Adverse events or other undesirable side effects caused by our product candidates could cause us, our collaborators, or regulatory authorities to interrupt, delay, or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA, EMA, or other comparable foreign regulatory authorities.

Our most advanced product candidates, BIIB122/DNL151, DNL310, SAR443820/DNL788, and eclitasertib or SAR443122/DNL758, (SAR443122/DNL758), DNL343, and TAK-594/DNL593 are currently our only clinical stage product candidates. Adverse events and other side effects may result from higher dosing, repeated dosing, and/or longer-term exposure to our product candidates and could lead to delays and/or termination of the development of these product candidates.

On January 13, 2022, we announced that the TAK-290/DNL919 (ATV:TREM2) IND application had been placed on clinical hold by the FDA. In For example, in August 2023, we announced that, in agreement together with our collaboration partner Takeda, we will made the strategic decision to discontinue clinical development of TAK-920/DNL919 in Alzheimer's disease. This is a strategic decision based on the totality of clinical data emerging from the single ascending dose Phase 1 study of TAK-920/DNL919 in healthy volunteers and in consideration of the rapidly evolving treatment landscape for Alzheimer's disease whereby an understanding of drug combinations with newly approved therapies will be important.following a clinical hold by the FDA.

In 2020, we paused clinical studies with DNL747 in our RIPK1 program. Chronic toxicity studies with DNL747 in cynomolgus monkeys showed dose- and duration-dependent adverse preclinical findings at exposures higher than those tested in the clinic. These findings, which are considered off-target and molecule-specific, may impact the ability to increase the dose of DNL747 and achieve higher levels of target inhibition without time consuming additional clinical safety studies in patients to evaluate the long-term safety and tolerability.

Drug-related side effects could affect patient recruitment, the ability of enrolled patients to complete the trial, and/or result in potential product liability claims. We are required to maintain product liability insurance pursuant to certain of our license agreements. We may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. A successful product liability claim or series of claims brought against us could cause our stock price to decline and, if judgments exceed our insurance coverage, could adversely affect our results of operations and business. In addition, regardless of merit or eventual outcome, product liability claims may result in impairment of our business reputation, withdrawal of clinical trial participants, costs due to related litigation, distraction of management's attention from our primary business, initiation of investigations by regulators, substantial monetary awards to patients or other claimants, the inability to commercialize our product candidates, and decreased demand for our product candidates, if approved for commercial sale.

Additionally, if one or more of our product candidates receives marketing approval, and we or others, including our collaborators, later identify undesirable side effects or adverse events caused by such products, a number of potentially significant negative consequences could result, including but not limited to:

- regulatory authorities may withdraw approvals of such product and cause us to recall our product;
- regulatory authorities may require additional warnings on the label;
- we may be required to change the way the product is administered or conduct additional clinical trials or post-approval studies;
- we may be required to create a Risk Evaluation and Mitigation Strategy plan to assure safe use;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, and could significantly harm our business, financial condition, results of operations, and growth prospects. We cannot predict whether our product candidates will cause toxicities in humans that would preclude or lead to the revocation of regulatory approval based on nonclinical studies or early-stage clinical trials.

We currently and may in the future conduct clinical trials for our product candidates outside the United States, and the FDA, EMA, and applicable foreign regulatory authorities may not accept data from such trials.

We currently conduct clinical trials outside the United States, including in Europe, and may continue to do so in the future. The acceptance of data from clinical trials conducted outside the United States or another jurisdiction by the FDA, EMA, or applicable foreign regulatory authority may be subject to certain conditions. In cases where data from foreign clinical trials are intended to serve as the basis for marketing approval in the United States, the FDA will generally not approve the application on the basis of foreign data alone unless (i) the data are applicable to the United States population and United States medical practice; and (ii) the trials were performed by clinical investigators of recognized competence and pursuant to cGCP regulations. Additionally, the FDA's clinical trial requirements, including sufficient size of patient populations and statistical powering, must be met. Many foreign regulatory bodies have similar approval requirements. In addition, such foreign trials would be subject to the applicable local laws of the foreign jurisdictions where the trials are conducted. There can be no assurance that the FDA, EMA, or any applicable foreign regulatory authority will accept data from trials conducted outside of the United States or the applicable jurisdiction. If the FDA, EMA, or any applicable foreign regulatory authority does not accept such data, it would result in the need for additional trials, which would be costly and time-consuming and delay aspects of our business plan, and which may result in our product candidates not receiving approval or clearance for commercialization in the applicable jurisdiction.

Obtaining and maintaining regulatory approval of our product candidates in one jurisdiction does not mean that we will be successful in obtaining regulatory approval of our product candidates in other jurisdictions.

Obtaining and maintaining regulatory approval of our product candidates in one jurisdiction does not guarantee that we will be able to obtain or maintain regulatory approval in any other jurisdiction, and a failure or delay in obtaining regulatory approval in one jurisdiction may have a negative effect on the regulatory approval process in others. For example, even if the FDA or EMA grants marketing approval of a product candidate, comparable regulatory authorities in foreign jurisdictions must also approve the manufacturing, marketing, and promotion of the product candidate in those countries. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from those in the United States, including additional preclinical studies or clinical trials as clinical trials conducted in one jurisdiction may not be accepted by regulatory authorities in other jurisdictions. In many jurisdictions outside the United States, a product candidate must be approved for reimbursement before it can be approved for sale in that jurisdiction. In some cases, the price that we intend to charge for our products is also subject to approval.

Obtaining foreign regulatory approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties, and costs for us and could delay or prevent the introduction of our products in certain countries. If we or any partner we work with fail to comply with the regulatory requirements in international markets or fail to receive applicable marketing approvals, our target market will be reduced and our ability to realize the full market potential of our product candidates will be harmed.

Even if we obtain regulatory approval for a product candidate, our products will remain subject to extensive regulatory scrutiny.

If any of our product candidates are approved, they will be subject to ongoing regulatory requirements, including both federal and state requirements in the United States and requirements of comparable foreign regulatory authorities.

While healthcare professionals are free to use and prescribe drug products for off-label uses, the FDA strictly regulates manufacturers' promotional claims of drug products. In particular, a product may not be promoted for uses that are not approved by the FDA as reflected in the FDA-approved labeling. A company that is found to have improperly promoted off-label uses may be subject to large civil and criminal fines, penalties, and enforcement actions. If we cannot successfully manage the promotion of our approved product candidates, we could become subject to significant liability, which would could materially adversely affect our business and financial condition.

Manufacturers and manufacturers' facilities are required to comply with extensive requirements imposed by the FDA, EMA and comparable foreign regulatory authorities, including ensuring that quality control and manufacturing procedures conform to cGMP regulations.

Any regulatory approvals that we receive for our product candidates will be subject to limitations on the approved indicated uses for which the product may be marketed and promoted or to the conditions of approval (including the requirement to implement a Risk Evaluation and Mitigation Strategy) or contain requirements for potentially costly post-marketing testing. We will be required to report certain adverse reactions and production problems, if any, to the FDA, EMA, and comparable foreign regulatory authorities. Any new legislation addressing drug safety issues could result in delays in product development or commercialization, or increased costs to assure compliance. The FDA and other agencies, including the Department of Justice, closely regulate and monitor the post-approval marketing and promotion of products to ensure that they are manufactured, marketed, and distributed only for the approved indications and in accordance with the provisions of the approved labeling. We will have to comply with requirements concerning advertising and promotion for our products. Promotional communications with respect to prescription drugs are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved label. As such, we may not promote our products for indications or uses for which they do not have approval. The holder of an approved NDA, BLA, or MAA must submit new or supplemental applications and obtain approval for certain changes to the approved product, product labeling, or manufacturing process. We could also be asked to conduct post-marketing clinical trials to verify the safety and efficacy of our non-biologic products or safety, purity, and potency for our biologic products, in general or in specific patient subsets. If original marketing approval was obtained via the accelerated approval pathway, we could be required to conduct a successful post-marketing clinical trial to confirm clinical benefit for our products. Further, in December 2022, the Consolidated Appropriations Act, 2023, including the The Food and Drug Omnibus Reform Act (FDORA), was signed into law. FDORA made several changes to the FDA's authorities and its regulatory framework, including, among other changes, reforms to reformed the accelerated approval pathway, such as requiring the FDA to specify conditions for post-approval study requirements and setting forth procedures for the FDA to withdraw a product on an expedited basis for non-compliance with post-approval requirements. An unsuccessful post-marketing study or failure to complete such a study could result in the withdrawal of marketing approval.

Manufacturers and manufacturers' facilities are required to comply with extensive requirements imposed by the FDA, EMA, and comparable foreign regulatory authorities, including ensuring that quality control and manufacturing procedures conform to cGMP regulations. If a regulatory agency discovers previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, or disagrees with the promotion, marketing, or labeling of a product, such regulatory agency may impose restrictions on that product or us, including requiring withdrawal of the product from the market. If we fail to comply with applicable regulatory requirements, a regulatory agency or enforcement authority may, among other things, issue warning letters, impose penalties, suspend regulatory approvals, or require a product recall. Any of these actions by a regulatory agency could require us to expend significant time and resources, generate negative publicity, and adversely affect the value of our company.

We have received orphan drug designation from ***To the FDA for DNL310, and plan to extent we seek orphan drug designation for additional any of our product candidates, but we may be unable to obtain such designations or to maintain the benefits associated with orphan drug status, including market exclusivity, which may cause our revenue, if any, to be reduced.***

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biologic intended to treat a rare disease or condition where there is no reasonable expectation that the cost of developing and making available the drug or biologic in the United States will be recovered from sales in the United States for that drug or biologic. Once granted, orphan drug designation entitles a party to financial incentives and certain exclusivity protections. In February 2019, the FDA granted orphan drug designation for our DNL310 program in Hunter syndrome. However, the FDA can still approve other drugs that have a different active ingredient for use in treating the same indication or disease, and can waive orphan exclusivity if we are unable to manufacture sufficient supply of our product. We plan to seek orphan drug designations for some other product candidates, but we may be unable to obtain such designations.

Further, in response to *Catalyst Pharms., Inc. v. Becerra*, 14 F.4th 1299 (11th Cir. 2021), the court disagreed with the FDA's longstanding position FDA clarified in a January 2023 notice that the orphan drug exclusivity only applies to the approved use or indication within an eligible disease, and not to all uses or indications within the entire disease or condition. In particular, the circuit court held that the orphan-drug exclusivity for Catalyst's drug blocked FDA's approval of another drug for all uses or indications within the same orphan-designated disease, or Lambert-Eaton myasthenic syndrome (LEMS), even though Catalyst's drug was approved at that time only for use in the treatment of LEMS in adults. Accordingly, the court ordered the FDA to set aside the approval of a drug indicated for LEMS in children. This decision created uncertainty in the application of the orphan drug exclusivity. On January 24, 2023, the FDA published a notice in the Federal Register to clarify that while the agency complies with the court's order in Catalyst, the FDA intends to continue to apply its longstanding interpretation of the regulations to matters outside of the scope of the Catalyst order – that is, the agency will continue tying the scope of orphan-

drug exclusivity to the uses or indications for which a drug is approved, which permits other sponsors to obtain approval of a drug for new uses or indications within the same orphan designated disease or condition that have not yet been approved. It is unclear how future litigation, legislation, agency decisions, and administrative actions will impact the scope of the orphan drug exclusivity.

We have received Fast Track designation from the FDA for SAR443820/DNL788 and may seek Fast Track designation from the FDA for additional product candidates. Even if one or more of our product candidates receives Fast Track designation, we may be unable to obtain or maintain the benefits associated with the Fast Track designation.

The FDA has granted Fast Track designation to SAR443820/DNL788. Fast Track designation is designed to facilitate the development and expedite the review of therapies to treat serious conditions and fill an unmet medical need. However, if we do not continue to meet the criteria of the Fast Track designation, or if our clinical trials are delayed, suspended or terminated, or put on clinical hold due to unexpected adverse events or issues with clinical supply, we will not receive the benefits associated with the Fast Track program. Furthermore, Fast Track designation does not change the standards for approval. Fast Track designation alone does not guarantee qualification for the FDA's priority review procedures. Fast track designation also does not guarantee our product candidate will be approved in a timely manner, if at all.

Healthcare legislative measures aimed at reducing healthcare costs may have a material adverse effect on our business and results of operations.

We may face difficulties from changes to current regulations and future legislation. Current and future legislation may increase the difficulty and cost for us to commercialize our drugs, if approved, and affect the prices we may obtain, including changes in coverage and reimbursement policies in certain market segments for our product candidates, which could make it difficult for us to sell our product candidates, if approved, profitably. Third-party payors, whether domestic or foreign, or governmental or commercial, are developing increasingly sophisticated methods of controlling healthcare costs.

In both the United States and certain foreign jurisdictions, there have been a number of legislative and regulatory changes to the health care system that could impact our ability to sell our products profitably. These include the enactment of the Affordable Care Act of 2010 (“ACA”), the American Rescue Plan Act of 2021, which will eliminate a statutory cap on Medicaid Drug Rebate Program rebates that manufacturers pay to state Medicaid programs, and the July 2021 executive order, "Promoting Competition in the American Economy," with multiple provisions aimed at increasing competition for prescription drugs. In August 2022, Congress passed the Inflation Reduction Act of 2022 ("IRA"), which includes prescription drug provisions that have significant implications for the pharmaceutical industry and Medicare beneficiaries, including allowing the federal government to negotiate a maximum fair price for certain high-priced single source Medicare drugs, imposing penalties and excise tax for manufacturers that fail to comply with the drug price negotiation requirements, requiring inflation rebates for all Medicare Part B and Part D drugs, with limited exceptions, if their drug prices increase faster than inflation, and redesigning Medicare Part D to reduce out-of-pocket prescription drug costs for beneficiaries, among other changes. Various industry stakeholders, including pharmaceutical companies, the U.S. Chamber of Commerce, and the Pharmaceutical Research and Manufacturers of America, have initiated lawsuits against the federal government asserting that the price negotiation provisions of the Inflation Reduction Act ("IRA") are unconstitutional. The impact of these judicial changes, legislative, executive, and administrative actions and any future healthcare measures and agency rules implemented by the government on us and the pharmaceutical industry as a whole is unclear. At the state level, a number of states are considering or have recently enacted state drug price transparency and reporting laws that could substantially increase our compliance burdens and expose us to greater liability under such state laws once we begin commercialization after obtaining regulatory approval for any of our products.

Since its enactment, there have been executive, judicial and Congressional congressional challenges to certain aspects of the ACA. ACA and IRA. It is unclear how future litigation or healthcare measures promulgated by the Biden administration will impact our business, financial condition, and results of operations. Complying with any new legislation or changes in healthcare regulation could be time-intensive and expensive, resulting in material adverse effect on our business. We expect that the ACA and IRA, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, lower reimbursement, and new payment methodologies. This could lower the price that we receive for any approved product. Any denial in coverage or reduction in reimbursement from Medicare or other government-funded programs may result in a similar denial or reduction in payments from private payors, which may prevent us from being able to generate sufficient revenue, attain profitability or commercialize our product candidates, if approved. In addition, increased scrutiny by the U.S. Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

There have been, and likely will continue to be, legislative and regulatory proposals at the foreign, federal and state levels directed at containing or lowering the cost of healthcare. We cannot predict the initiatives that may be adopted in the future. The continuing efforts of the government, insurance companies, managed care organizations, and other payors of healthcare services to contain or reduce costs of healthcare and/or impose price controls may adversely affect the demand for any product candidates that are approved, our ability to receive or set a price we believe is fair for our products, our ability to attract investment, our ability to generate revenue or achieve profitability, the level of taxes we are required to pay, and the availability of capital.

Our employees, independent contractors, consultants, commercial partners, and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.

We are exposed to the risk of fraud, misconduct, or other illegal activity by our employees, independent contractors, consultants, commercial partners, and vendors. Misconduct by these parties could include intentional, reckless, and negligent conduct that fails to: comply with the laws of the FDA, EMA, and other comparable foreign regulatory authorities; provide true, complete, and accurate information to regulatory authorities; comply with manufacturing standards we have established; comply with healthcare fraud and abuse laws in the United States and similar foreign fraudulent misconduct laws; or report financial information or data accurately or to disclose unauthorized activities to us. If we

obtain FDA approval of any of our product candidates and begin commercializing those products in the United States, our potential exposure under such laws will increase significantly, and our costs associated with compliance with such laws are also likely to increase. In particular, research, sales, marketing, education, and other business arrangements in the healthcare industry are subject to extensive laws designed to prevent fraud, kickbacks, self-dealing, and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, educating, marketing and promotion, sales and commission, certain customer incentive programs, and other business arrangements generally. Activities subject to these laws also involve the improper use of information obtained in the course of patient recruitment for clinical trials, which could result in regulatory sanctions and cause serious harm to our reputation. We have adopted a code of business conduct and ethics, but it is not always possible to identify and deter misconduct by employees and third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions.

If we fail to comply with healthcare laws, we could face substantial penalties and our business, operations, and financial conditions could be adversely affected.

If we obtain FDA approval for any of our product candidates and begin commercializing those products in the United States, our operations will be subject to various federal, state, local, and foreign healthcare fraud and abuse laws. The laws that may impact our operations include the federal Anti-Kickback Statute, the False Claims Act, the federal Health Insurance Portability and Accountability Act of 1996 ("HIPAA"), as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 ("HITECH"), the federal Physician Payment Sunshine Act, federal consumer protection and unfair competition laws, and analogous state and foreign laws and regulations. These laws may impact, among other things, our clinical research program, as well as our proposed and future sales, marketing, and education programs. In particular, the promotion, sales, and marketing of healthcare items and services is subject to extensive laws and regulations designed to prevent fraud, kickbacks, self-dealing, and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive, and other business arrangements.

Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our business activities could, despite our efforts to comply, be subject to challenge under one or more of such laws. Efforts to ensure that our business arrangements will comply with applicable healthcare laws may involve substantial costs. It is possible that governmental and enforcement authorities will conclude that our business practices may not comply with current or future statutes, regulations, or case law interpreting applicable fraud and abuse or other healthcare laws and regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of civil, criminal, and administrative penalties, damages, disgorgement, monetary fines, possible exclusion from participation in Medicare, Medicaid, and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations. In addition, the approval and commercialization of any of our product candidates outside the United States will also likely subject us to foreign equivalents of the healthcare laws mentioned above, among other foreign laws.

Our business is subject to complex and evolving U.S. and foreign laws and regulations, information security policies, and contractual obligations relating to privacy and data protection, including the use, processing, and cross-border transfer of personal information. These laws and regulations are subject to change and uncertain interpretation, and could result in claims, changes to our business practices, or monetary penalties, and otherwise may harm our business.

We receive, generate, and store significant and increasing volumes of sensitive information and business-critical information, including employee and personal data (including protected health information), research and development information, commercial information, and business and financial information. We heavily rely on external security and infrastructure vendors to manage our information technology systems and data centers. We face a number of risks relative to protecting this critical information, including the loss of access, inappropriate use or disclosure, inappropriate modification, and the risk of our being unable to adequately monitor, audit, and modify our controls over our critical information. This risk extends to third-party vendors and subcontractors we use to manage this sensitive data.

A wide variety of provincial, state, national, and international laws and regulations apply to the collection, use, retention, protection, disclosure, transfer, and other processing of personal data. These laws and regulations are evolving and may result in ever-increasing regulatory and public scrutiny and escalating levels of enforcement and sanctions. For example, the collection and use of personal data in the EU are governed by the EU General Data Protection Regulation ("GDPR"), which became fully effective on May 25, 2018. The GDPR imposes stringent data protection requirements, including, for example, more robust disclosures to individuals and a strengthened individual data rights regime, shortened timelines for data breach notifications, limitations on retention of information, increased requirements pertaining to special categories of data, such as health data, and additional obligations when we contract with third-party processors in connection with the processing of the personal data. The GDPR also imposes strict rules on the transfer of personal data out of the EU to the United States and other countries, and in the context of clinical trials we currently rely on patient informed consent as the legal basis for such transfers. In addition, the GDPR provides that EU member states may make their own further laws and regulations limiting the processing of personal data, including genetic, biometric or health data. The GDPR provides for penalties for noncompliance of up to the greater of €20 million or four percent of worldwide annual revenues. The GDPR applies extraterritorially, and we may be subject to the GDPR because of our data processing activities that involve the personal data of individuals located in the EU, such as in connection with any EU clinical trials. Additionally, the UK has implemented legislation that substantially implements the GDPR (the "UK GDPR"), with substantial penalties for noncompliance of up to the greater of £17.5 million or four percent of worldwide revenues. Aspects of UK data protection laws and regulations remain unclear. On June 28, 2021, the European Commission announced a decision of "adequacy" concluding that the UK ensures an equivalent level of data protection to the GDPR, which provides some relief regarding the legality of continued personal data flows from the European Economic Area ("EEA") to the UK. Some uncertainty remains, however, as this adequacy determination must be renewed after four years and may be modified or revoked in the interim. We cannot fully predict how the UK GDPR and data protection laws or regulations may develop in the medium-to-long term. noncompliance.

We may incur liabilities, expenses, costs, and other operational losses under the GDPR and UK GDPR as well as privacy and data protection laws of Switzerland, the United Kingdom, and applicable EU member states. We may find it necessary or appropriate to make additional changes to the ways we or our service providers collect, disclose, transfer, and otherwise process data within the EEA, Switzerland, and the UK, and to our related policies and practices. This may be onerous and may interrupt or delay our development activities, and adversely affect our business, financial condition, results of operations and prospects.

Further, various states, such as California, Massachusetts, and Massachusetts, Washington have implemented similar privacy laws and regulations that impose restrictive requirements regulating the use and disclosure of health information and other personally identifiable personal information. Where state laws are more protective than HIPAA, we must comply with the stricter provisions. In addition to fines and penalties imposed upon violators, some of these state laws also afford private rights of action to individuals who believe their personal information has been misused. For example, California has enacted legislation, the California Consumer Privacy Act ("CCPA"), that, among other things, requires covered companies to provide new disclosures to California consumers, and affords such consumers new abilities to opt-out of certain sales of personal information. Other states in the United States have proposed or enacted similar legislation, including enacted legislation in Colorado, Virginia, Utah, and Connecticut that has or will become effective in 2023. The CCPA became effective on January 1, 2020. The CCPA, as amended and expanded by the California Privacy Rights Act ("CPRA"), requires covered companies to provide new disclosures to individuals and consumers in California, and afford such individuals and consumers new data protection rights, including the ability to opt-out of certain sales of personal information. Numerous other states in the United States have proposed or enacted similar legislation. Further, some states have enacted more specific legislation, such as Washington's enactment of the My Health, My Data Act, which includes a private right of action. The U.S. federal government is also contemplating federal privacy legislation. The GDPR, UK GDPR, CCPA, CPRA, and many other federal, state, and foreign laws and regulations relating to privacy and data protection are still being tested in courts, and they are subject to new and differing interpretations by courts and regulatory officials. The U.S. federal government is also contemplating federal privacy legislation. Additionally, the interplay of federal and state laws may be subject to varying interpretations by courts and government agencies, creating complex compliance issues for us and data we receive, use and share, potentially exposing us to additional expense, adverse publicity and liability. We are working to comply with the GDPR, UK GDPR, CCPA, CPRA and other privacy and data protection laws and regulations that apply to us, and we anticipate needing to devote significant additional resources to complying with these laws and regulations. These and future laws and regulations may increase our compliance costs and potential liability.

It is possible that the GDPR, UK GDPR, CCPA, CPRA, or other laws and regulations relating to privacy and data protection may be interpreted and applied in a manner that is inconsistent from jurisdiction to jurisdiction or inconsistent with our current policies and practices. We cannot guarantee that we are in compliance with all such applicable data protection laws and regulations and we cannot be sure how these regulations will be interpreted, enforced or applied to our operations. Furthermore, other jurisdictions outside the EU are similarly introducing or enhancing privacy and data security laws, rules, and regulations, which could increase our compliance costs and the risks associated with noncompliance. It is possible that these laws may be interpreted and applied in a manner that is inconsistent with our practices and our efforts to comply with the evolving data protection rules may be unsuccessful. We cannot guarantee that we or our vendors may be in compliance with all applicable international laws and regulations as they are enforced now or as they evolve. For example, our privacy policies may be insufficient to protect any personal information we collect, or may not comply with applicable laws. Our non-compliance could result in government-imposed fines or orders requiring that we change our practices, which could adversely affect our business. In addition to the risks associated with enforcement activities and potential contractual liabilities, our ongoing efforts to comply with evolving laws and regulations at the federal and state level may be costly and require ongoing modifications to our policies, procedures and systems. In addition, if we are unable to properly protect the privacy and security of protected health information, we could be alleged or found to have breached our contracts.

Our actual or perceived failure to adequately comply with applicable laws and regulations or other actual or asserted obligations relating to privacy and data protection, or to protect personal data and other data we process or maintain, could result in regulatory enforcement actions against us, including fines, imprisonment of company officials and public censure, claims for damages by affected individuals, other lawsuits or reputational and damage, all of which could materially affect our business, financial condition, results of operations and growth prospects.

If we or any contract manufacturers and suppliers we engage fail to comply with environmental, health, and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.

We and any contract manufacturers and suppliers we engage are subject to numerous federal, state, and local environmental, health, and safety laws, regulations, and permitting requirements, including those governing laboratory procedures; the generation, handling, use, storage, treatment, and disposal of hazardous and regulated materials and wastes; the emission and discharge of hazardous materials into the ground, air, and water; and employee health and safety. Our operations involve the use of hazardous and flammable materials, including chemicals and biological and radioactive materials. Our operations also produce hazardous waste. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. Under certain environmental laws, we could be held responsible for costs relating to any contamination at our current or past facilities and at third-party facilities. We also could incur significant costs associated with civil or criminal fines and penalties.

Compliance with applicable environmental laws and regulations may be expensive, and current or future environmental laws and regulations may impair our research, product development, and manufacturing efforts. In addition, we cannot entirely eliminate the risk of accidental injury or contamination from these materials or wastes. Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not carry specific biological or hazardous waste insurance coverage, and our property, casualty, and general liability insurance policies specifically exclude coverage for damages and fines arising from biological or hazardous waste exposure or contamination. Accordingly, in the event of contamination or injury, we could be held liable for damages or be penalized with fines in an amount exceeding our resources, and our clinical trials or regulatory approvals could be suspended, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

Our business activities may be subject to the Foreign Corrupt Practices Act and similar anti-bribery and anti-corruption laws, as well as U.S. and certain foreign export controls, trade sanctions, and import laws and regulations.

Our business activities may be subject to the Foreign Corrupt Practices Act of 1977, as amended (the "FCPA"), and similar anti-bribery or anti-corruption laws, regulations, or rules of other countries in which we operate, including the U.K. Bribery Act. The FCPA generally prohibits offering, promising, giving, or authorizing others to give anything of value, either directly or indirectly, to a non-U.S. government official in order to influence official action, or otherwise obtain or retain business. The FCPA also requires public companies to make and keep books and records that accurately and fairly reflect the certain transactions of the corporation and to devise and maintain an adequate system of internal accounting controls. Our business is heavily regulated and therefore involves significant interaction with public officials, including officials of non-U.S. governments. Additionally, in many other countries, the health care providers who prescribe pharmaceuticals are employed by their government, and the purchasers of pharmaceuticals are government entities; therefore, our dealings with these prescribers and purchasers are subject to regulation under the FCPA. Recently the Securities and Exchange Commission (the "SEC"), and Department of Justice have increased their FCPA enforcement activities with respect to biotechnology and pharmaceutical companies. There is no certainty that all of our employees, agents, contractors, or collaborators, or those of our affiliates, will comply with all applicable laws and regulations, particularly given the high level of complexity of these laws. Violations of these laws and regulations could result in fines, criminal sanctions against us, our officers, or our employees, the closing down of our facilities, requirements to obtain export licenses, cessation of business activities in sanctioned countries, implementation of compliance programs, and prohibitions on the conduct of our business. Any such violations could include prohibitions on our ability to offer our products in one or more countries and could materially damage our reputation, our brand, our international expansion efforts, our ability to attract and retain employees, and our business, prospects, operating results, and financial condition.

In addition, in the future once we enter a commercialization phase, our products may be subject to U.S. and foreign export controls, trade sanctions and import laws and regulations. Governmental regulation of the import or export of our products, or our failure to obtain any required import or export authorization for our products, when applicable, could harm our international sales and adversely affect our revenue. Compliance with applicable regulatory requirements regarding the export of our products may create delays in the introduction of our products in international markets or, in some cases, prevent the export of our products to some countries altogether. Furthermore, U.S. export control laws and economic sanctions prohibit the shipment of certain products and services to countries, governments, and persons targeted by U.S. sanctions. If we fail to comply with export and import regulations and such economic sanctions, we may be fined or other penalties could be imposed, including a denial of certain export privileges. Moreover, any new export or import restrictions, new legislation or shifting approaches in the enforcement or scope of existing regulations, or in the countries, persons, or technologies targeted by such regulations, could result in decreased use of our products by, or in our decreased ability to export our products to existing or potential customers with international operations. Any limitation on our ability to export or sell access to our products would likely adversely affect our business.

Inadequate funding for the FDA, the SEC and other government agencies could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner, or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory, and policy changes. Average review times at the FDA have fluctuated in recent years as a result. In addition, government funding of the SEC and other government agencies on which our operations may rely, including those that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other government agencies may also slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years the U.S. government shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical government employees and stop critical activities. While the FDA has largely caught up with domestic preapproval inspections since the start of the COVID-19 pandemic, it continues to work through its backlog of foreign inspections. However, if If a prolonged government shutdown or other disruption occurs, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, or to provide feedback on our clinical development plans, which could have a material adverse effect on our business. Further, future government shutdowns or other disruptions to normal operations could impact our ability to access the public markets and obtain the funding necessary to properly capitalize and continue our operations.

Risks Related to Our Reliance on Third Parties

We depend on collaborations with third parties for the research, development, and commercialization of certain product candidates. If any such collaborations are not successful, we may not be able to realize the market potential of those product candidates.

We anticipate seeking third-party collaborators for the research, development, and commercialization of certain of the product candidates we may develop. For example, we have collaborations with F-star, Takeda, Sanofi, Biogen, and others to further our development of product candidates and to enhance our research efforts directed to better understanding neurodegenerative and lysosomal storage diseases. Our likely collaborators for any other collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies, biotechnology companies, and academic institutions. If we enter into any such arrangements with any third parties, we will likely have shared or limited control over the amount and timing of resources that our collaborators dedicate to the development or potential commercialization of any product candidates we may seek to develop with them. Our ability to generate revenue from these arrangements with commercial entities will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements. We cannot predict the success of any collaboration that we enter into.

Collaborations involving our research programs, or any product candidates we may develop, pose the following risks to us:

- collaborators generally have significant discretion in determining the efforts and resources that they will apply to these collaborations;

- collaborators may not properly obtain, maintain, enforce, or defend intellectual property or proprietary rights relating to our product candidates or research programs or may use our proprietary information in such a way as to expose us to potential litigation or other intellectual property related proceedings, including proceedings challenging the scope, ownership, validity and enforceability of our intellectual property;

- collaborators may own or co-own intellectual property covering our product candidates or research programs that results from our collaboration with them, and in such cases, we may not have the exclusive right to commercialize such intellectual property or such product candidates or research programs;

- we may need the cooperation of our collaborators to enforce or defend any intellectual property we contribute to or that arises out of our collaborations, which may not be provided to us;

- collaborators may control certain interactions with regulatory authorities, which may impact on our ability to obtain and maintain regulatory approval of our products candidates;

- disputes may arise between the collaborators and us that result in the delay or termination of the research, development, or commercialization of our product candidates or research programs or that result in costly litigation or arbitration that diverts management attention and resources;

- collaborators may decide to not pursue development and commercialization of any product candidates we develop or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborator's strategic focus or available funding or external factors such as an acquisition that diverts resources or creates competing priorities;

- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials, or require a new formulation of a product candidate for clinical testing;

- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates or research programs if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;

- collaborators may restrict us from researching, developing, or commercializing certain products or technologies without their involvement;

- collaborators with marketing and distribution rights to one or more product candidates may not commit sufficient resources to the marketing and distribution of such product candidates;

- we may lose certain valuable rights under circumstances identified in our collaborations, agreements with our collaborators, including if we undergo a change of control;

- collaborators may grant sublicenses to our technology or product candidates or undergo a change of control and the sublicensees or new owners may decide to take the collaboration in a direction which is not in our best interest;

- collaborators may become bankrupt, which may significantly delay our research or development programs, or may cause us to lose access to valuable technology, know-how, or intellectual property of the collaborator relating to our products, product candidates, or research programs;

- key personnel at our collaborators may leave, which could negatively impact our ability to productively work with our collaborators;

- collaborations may require us to incur short and long-term expenditures, issue securities that dilute our stockholders, or disrupt our management and business;

- if our collaborators do not satisfy their obligations under our agreements with them, or if they terminate our collaborations with them, we may not be able to develop or commercialize product candidates as planned;

- collaborations may require us to share in development and commercialization costs pursuant to budgets that we do not fully control and our failure to share in such costs could have a detrimental impact on the collaboration or our ability to share in revenue generated under the collaboration;

- collaborations may be terminated in their entirety or with respect to certain product candidates or technologies and, if so terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates or technologies, including our BBB platform technology; and

- collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all. If a present or future collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our development or commercialization program under such collaboration could be delayed, diminished, or terminated.

We may face significant competition in seeking appropriate collaborations. Recent business combinations among biotechnology and pharmaceutical companies have resulted in a reduced number of potential collaborators. In addition, the negotiation process is time-consuming and complex, and we may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of the product candidate for which we are seeking to collaborate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop product candidates or bring them to market and generate product revenue.

If we enter into collaborations to develop and potentially commercialize any product candidates, we may not be able to realize the benefit of such transactions if we or our collaborator elects not to exercise the rights granted under the agreement or if we or our collaborator are unable to successfully integrate a product candidate into existing operations and company culture. The failure to develop and commercialize a product candidate pursuant to our agreements with our current or future collaborators could prevent us from receiving future payments under such agreements, which could negatively impact our revenues. In addition, if our agreement with any of our collaborators terminates, our access to technology and intellectual property licensed to us by that collaborator may be restricted or terminate entirely, which may delay our continued development of our product candidates utilizing the collaborator's technology or intellectual property or require us to stop development of those product candidates completely. We may also find it more difficult to find a suitable replacement collaborator or attract new collaborators, and our development programs may be delayed or the perception of us in the business and financial communities could be adversely affected. Many of the risks relating to product development, regulatory approval, and commercialization described in this "Risk Factors" section also apply to the activities of our collaborators and any negative impact on our collaborators may adversely affect us.

We rely on third parties to conduct our clinical trials and some aspects of our research and preclinical testing, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials, research, or testing.

We currently rely and expect to continue to rely on third parties, such as CROs, clinical data management organizations, medical institutions, and clinical investigators, to conduct some aspects of our research and preclinical testing and our clinical trials. Any of these third parties may terminate their engagements with us or be unable to fulfill their contractual obligations. If we need to enter into alternative arrangements, it would delay our product development activities.

Our reliance on these third parties for research and development activities reduces our control over these activities but does not relieve us of our responsibilities. For example, we remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with cGCPs for conducting, recording, and reporting the results of clinical trials to assure that data and reported results are credible, reproducible, and accurate and that the rights, integrity, and confidentiality of trial participants are protected. We also are required to register ongoing clinical trials and post the results of completed clinical trials on a government-sponsored database within certain time frames. Failure to do so can result in fines, adverse publicity, and civil and criminal sanctions.

Our third-party service providers are not our employees, and we are therefore unable to directly monitor whether or not they devote sufficient time and resources to our clinical and nonclinical programs. These third-party service providers may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other drug development activities that could harm our competitive position. If these third parties do not successfully carry out their contractual duties, meet expected deadlines, or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, marketing approvals for any product candidates we may develop and will not be able to, or may be delayed in our efforts to, successfully commercialize our medicines.

We also expect to rely on other third parties to store and distribute drug supplies for our clinical trials. Any performance failure on the part of our distributors, including with the shipment of any drug supplies, could delay clinical development or marketing approval of any product candidates we may develop or commercialization of our medicines, producing additional losses and depriving us of potential product revenue.

Our reliance on third parties for the manufacture of the significant majority of the materials for our research programs, preclinical studies, and clinical trials may increase the risk that we will not have sufficient quantities of such materials, product candidates, or any medicines that we may develop and commercialize, or that such supply will not be available to us at an acceptable cost, which could delay, prevent, or impair our development or commercialization efforts.

Although we have initiated the build-out of our Utah site to expand our clinical manufacturing capabilities for biologic therapeutics, we do not have any operational manufacturing facilities. We currently rely on third-party manufacturers for the manufacture of our materials for preclinical studies and clinical trials and expect to continue to do so for some or all of our materials for preclinical studies, clinical trials, and for commercial supply of any product candidates that we may develop.

We may be unable to establish any further agreements with third-party manufacturers or to do so on acceptable terms. Even if we are able to establish agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including the possible breach, termination, or non-renewal of the agreement by the third party, which may be costly or inconvenient, and the inability of the third party to produce the required volume in a timely manner. We may also be exposed to the risks of relying on the third party for regulatory compliance, quality assurance, safety, and pharmacovigilance and related reporting.

Third-party manufacturers may not be able to comply with U.S. export control regulations, cGMP regulations, or similar regulatory requirements outside the United States. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in a need to replace current third-party manufacturers including the possibility of supply delays, clinical holds on our trials, sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocations, seizures or recalls of product candidates or medicines, operating restrictions, and criminal prosecutions, any of which could significantly and adversely affect supplies of our medicines and harm our business, financial condition, results of operations, and growth prospects.

Any medicines that we may develop may compete with other product candidates and products for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us.

Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval. We do not currently have arrangements in place for redundant supply for many components of our product candidates. If any one of our current contract manufacturers cannot perform as agreed, we may be required to replace that manufacturer and may incur added costs and delays in identifying and qualifying any such replacement. Furthermore, securing and reserving production capacity with contract manufacturers may result in significant costs.

Our current and anticipated future dependence upon others third parties for the manufacture of any product candidates we may develop or medicines may adversely affect our future profit margins and our ability to commercialize any medicines that receive marketing approval on a timely and competitive basis.

We depend on third-party suppliers for key raw materials used in our manufacturing processes, and the loss of these third-party suppliers or their inability to supply us with adequate raw materials could harm our business.

We rely on third-party suppliers for the raw materials required for the production of our product candidates. Our dependence on these third-party suppliers and the challenges we may face in obtaining adequate supplies of raw materials involve several risks, including limited control over pricing, availability, quality, and delivery schedules. As a small company, our negotiation leverage is limited and we are likely to get lower priority than our larger competitors. We cannot be certain that our suppliers will continue to provide us with the quantities of these raw materials that we require or satisfy our anticipated specifications and quality requirements.

Further, we have in the past and may in the future experience delayed shipments of raw materials due to interruptions relating to the aforementioned events. We may be unable to find a sufficient alternative supply channel in a reasonable time or on commercially reasonable terms. Any performance failure on the part of our suppliers could delay the development and potential commercialization of our product candidates, including limiting supplies necessary for clinical trials and regulatory approvals, which would have a material adverse effect on our business.

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain patent protection for any product candidates we develop or for our BBB platform technology, our competitors could develop and commercialize products or technology similar or identical to ours, and our ability to successfully commercialize any product candidates we may develop, and our technology may be adversely affected.

Our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries with respect to our BBB platform technology and any proprietary product candidates and other technologies we may develop. We seek to protect our proprietary position by in-licensing intellectual property and filing patent applications in the United States and abroad relating to our BBB platform technology, programs and product candidates, as well as other technologies that are important to our business. Given that the development of our technology and product candidates is at an early stage, our intellectual property portfolio with respect to certain aspects of our technology and product candidates is also at an early stage. In addition, we cannot be certain that any patents we own or in-license in the United States adequately cover the Fc domain portion of our BBB platform technology that binds to transferrin receptor, or adequately cover the antibodies, enzymes or proteins being developed in our ATV:TREM2, ETV:IDS, ETV:SGSH, ETV:IDUA, PTV:PGRN, ATV:Abeta, OTV, or other TV-enabled programs. We have filed or intend to file patent applications on these aspects of our technology and product candidates; however, there can be no assurance that any such patent applications will issue as granted patents. Furthermore, in some cases, we have only filed provisional patent applications on certain aspects of our technology and product candidates and each of these provisional patent applications is not eligible to become an issued patent until, among other things, we file a non-provisional patent application within twelve months of the filing date of the applicable provisional patent application. Any failure to file a non-provisional patent application within this timeline could cause us to lose the ability to obtain patent protection for the inventions disclosed in the associated provisional patent applications. Furthermore, in some cases, we may not be able to obtain issued claims covering compositions relating to our BBB platform technology, programs and product

candidates, as well as other technologies that are important to our business, and instead may need to rely on filing patent applications with claims covering a method of use and/or method of manufacture for protection of such BBB platform technology, programs, product candidates, and other technologies. There can be no assurance that any such patent applications will issue as granted patents, and even if they do issue, such patent claims may be insufficient to prevent third parties, such as our competitors, from utilizing our technology. Any failure to obtain or maintain patent protection with respect to our BBB platform technology, programs and product candidates could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

If any of our owned or in-licensed patent applications do not issue as patents in any jurisdiction, we may not be able to compete effectively.

Changes in either the patent laws or their interpretation in the United States and other countries may diminish our ability to protect our inventions, obtain, maintain, and enforce our intellectual property rights and, more generally, could affect the value of our intellectual property or narrow the scope of our owned and licensed patents. With respect to both in-licensed and owned intellectual property, we cannot predict whether the patent applications we and our licensors are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide sufficient protection from competitors or other third parties.

The patent prosecution process is expensive, time-consuming, and complex, and we may not be able to file, prosecute, maintain, enforce, or license all necessary or desirable patent applications at a reasonable cost or in a timely manner, including delays as a result of the COVID-19 pandemic impacting our or our licensors' operations. It is also possible that we will fail to identify patentable aspects of our research and development output in time to obtain patent protection. Although we enter into nondisclosure and confidentiality agreements with parties who have access to confidential or patentable aspects of our research and development output, any of these parties may breach the agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection. In addition, our ability to obtain and maintain valid and enforceable patents depends on whether the differences between our inventions and the prior art allow our inventions to be patentable over the prior art. Furthermore, publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot be certain that we or our licensors were the first to make the inventions claimed in any of our owned or licensed patents or pending patent applications, or that we or our licensors were the first to file for patent protection of such inventions.

If the scope of any patent protection we obtain is not sufficiently broad, or if we lose any of our patent protection, our ability to prevent our competitors from commercializing similar or identical technology and product candidates would be adversely affected.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions, and has been the subject of much litigation in recent years. As a result, the issuance, scope, validity, enforceability, and commercial value of our patent rights are highly uncertain. Our owned or in-licensed pending and future patent applications may not result in patents being issued which protect our BBB platform technology, product candidates or other technologies or which effectively prevent others from commercializing competitive technologies and product candidates.

Moreover, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. Even if patent applications we license or own currently or in the future issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors or other third parties from competing with us, or otherwise provide us with any competitive advantage. Any patents that we own or in-license may be challenged, narrowed, circumvented, or invalidated by third parties. Consequently, we do not know whether our BBB platform technology, product candidates or other technologies will be protectable or remain protected by valid and enforceable patents. Our competitors or other third parties may be able to circumvent our patents by developing similar or alternative technologies or products in a non-infringing manner which could materially adversely affect our business, financial condition, results of operations and growth prospects.

The issuance of a patent is not conclusive as to its inventorship, scope, validity, or enforceability, and our patents may be challenged in the courts or patent offices in the United States and abroad. We or our licensors may be subject to a third-party preissuance submission of prior art to the USPTO, or become involved in opposition, derivation, revocation, reexamination, post-grant and *inter partes* review, or interference proceedings or other similar proceedings challenging our owned or licensed patent rights. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate or render unenforceable, our owned or in-licensed patent rights, allow third parties to commercialize our BBB platform technology, product candidates or other technologies and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights. Moreover, we, or one of our licensors, may have to participate in interference proceedings declared by the USPTO to determine priority of invention or in post-grant challenge proceedings, such as oppositions in a foreign patent office, that challenge our or our licensor's priority of invention or other features of patentability with respect to our owned or in-licensed patents and patent applications. Such challenges may result in loss of patent rights, loss of exclusivity, or in patent claims being narrowed, invalidated, or held unenforceable, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our BBB platform technology, product candidates and other technologies. Such proceedings also may result in substantial cost and require significant time from our scientists and management, even if the eventual outcome is favorable to us. If we or our collaborators are unsuccessful in any such proceeding or other priority or inventorship dispute, we may be required to obtain and maintain licenses from third parties, including parties involved in any such interference proceedings or other priority or inventorship disputes. Such licenses may not be available on commercially reasonable terms or at all, or may be non-exclusive. If we are unable to obtain and maintain such licenses, we may need to cease the development, manufacture, and commercialization of one or more of the product candidates we may develop. The loss of exclusivity or the narrowing of our owned and licensed patent claims could limit our ability to stop others from using or commercializing similar or identical technology and products.

In addition, given the amount of time required for the development, testing, and regulatory review of new product candidates, patents protecting such product candidates might expire before or shortly after such product candidates are commercialized. As a result, our intellectual property may not provide us with sufficient rights to exclude others from

commercializing products similar or identical to ours.

Some of our owned and in-licensed patents and patent applications are, and may in the future be, co-owned with third parties. For example, we currently, and may in the future, co-own certain patents and patent applications relating to our BBB platform technology with F-star. In addition, certain of our licensors co-own the patents and patent applications we in-license with other third parties with whom we do not have a direct relationship. Our exclusive rights to certain of these patents and patent applications are dependent, in part, on inter-institutional or other operating agreements between the joint owners of such patents and patent applications, who are not parties to our license agreements. If our licensors do not have exclusive control of the grant of licenses under any such third-party co-owners' interest in such patents or patent applications or we are otherwise unable to secure such exclusive rights, such co-owners may be able to license their rights to other third parties, including our competitors, and our competitors could market competing products and technology. In addition, we may need the cooperation of any such co-owners of our patents in order to enforce such patents against third parties, and such cooperation may not be provided to us. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and growth prospects.

Our rights to develop and commercialize our BBB platform technology and product candidates are subject, in part, to the terms and conditions of licenses granted to us by others or licenses granted by us to others.

We are heavily reliant upon licenses to certain patent rights and proprietary technology from third parties that are important or necessary to the development of our BBB platform technology and product candidates. For example, in June 2016, we entered into a license agreement with Genentech pursuant to which we received an exclusive license to certain of Genentech's intellectual property relating to our LRRK2 program, including our BIIB122/DNL151 product candidate.

Our agreements with F-star and other license agreements may not provide exclusive rights to use certain licensed intellectual property and technology in all relevant fields of use and in all territories in which we may wish to develop or commercialize our technology and products in the future. For example, F-star retains the right to use itself, and to license to others, its modular antibody technology for any purpose other than the targets which we have agreed with F-star would or may be exclusively available to us. As a result, we may not be able to prevent competitors or other third parties from developing and commercializing competitive products that also utilizes technology that we have in-licensed.

In addition, subject to the terms of any such license agreements, we do not have the right to control the preparation, filing, prosecution and maintenance, and we may not have the right to control the enforcement, and defense of patents and patent applications covering the technology that we license from third parties. For example, under our agreements with F-star and Genentech, the licensors control prosecution and, in the case of F-star and in specified circumstances, enforcement of certain of the patents and patent applications licensed to us. Also, under our agreements with Takeda, Sanofi and Biogen, they control prosecution, and in specified circumstances, enforcement of certain of the patents and patent applications licensed to them. We cannot be certain that our in-licensed or out-licensed patents and patent applications that are controlled by our licensors or licensees will be prepared, filed, prosecuted, maintained, enforced, and defended in a manner consistent with the best interests of our business. If our licensors or licensees fail to prosecute, maintain, enforce, and defend such patents, or lose rights to those patents or patent applications, the rights we have licensed may be reduced or eliminated, our right to develop and commercialize our BBB platform technology and any of our product candidates that are subject of such licensed rights could be adversely affected, and we may not be able to prevent competitors from making, using and selling competing products. In addition, even where we have the right to control patent prosecution of patents and patent applications we have licensed to and from third parties, we may still be adversely affected or prejudiced by actions or inactions of our licensees, our licensors and their counsel that took place prior to the date upon which we assumed control over patent prosecution.

Furthermore, our owned and in-licensed patents may be subject to a reservation of rights by one or more third parties. For example, our license to certain intellectual property owned by Genentech is subject to certain research rights Genentech granted to third parties prior to our license agreement. In addition, certain of our in-licensed intellectual property relating to RIPK1 was funded in part by the U.S. government. As a result, the U.S. government may have certain rights to such intellectual property. When new technologies are developed with U.S. government funding, the U.S. government generally obtains certain rights in any resulting patents, including a non-exclusive license authorizing the U.S. government to use the invention or to have others use the invention on its behalf. The U.S. government's rights may also permit it to disclose the funded inventions and technology to third parties and to exercise march-in rights to use or allow third parties to use the technology we have licensed that was developed using U.S. government funding. The U.S. government may exercise its march-in rights if it determines that action is necessary because we fail to achieve practical application of the government-funded technology, or because action is necessary to alleviate health or safety needs, to meet requirements of federal regulations, or to give preference to U.S. industry. In addition, our rights in such inventions may be subject to certain requirements to manufacture products embodying such inventions in the United States in certain circumstances and if this requirement is not waived. Any exercise by the U.S. government of such rights or by any third party of its reserved rights could have a material adverse effect on our competitive position, business, financial condition, results of operations and growth prospects.

If we fail to comply with our obligations in the agreements under which we license intellectual property rights from third parties or otherwise experience disruptions to our business relationships with our licensors, we could lose license rights that are important to our business.

We have entered into license agreements with third parties and may need to obtain additional licenses from others to advance our research or allow commercialization of product candidates we may develop or our BBB platform technology. It is possible that we may be unable to obtain additional licenses at a reasonable cost or on reasonable terms, if at all. In that event, we may be required to expend significant time and resources to redesign our technology, product candidates, or the methods for manufacturing them or to develop or license replacement technology, all of which may not be feasible on a technical or commercial basis. If we are unable to do so, we may be unable to develop or commercialize the affected product candidates or continue to utilize our existing BBB platform technology, which could harm our business, financial condition, results of operations, and growth prospects significantly. We cannot provide any assurances that third-party patents do not exist which might be enforced against our current technology, including our

BBB platform technology, manufacturing methods, product candidates, or future methods or products resulting in either an injunction prohibiting our manufacture or future sales, or, with respect to our future sales, an obligation on our part to pay royalties and/or other forms of compensation to third parties, which could be significant.

In addition, each of our current license agreements, and we expect our future agreements, will impose various development, diligence, commercialization, and other obligations on us. Certain of our license agreements also require us to meet development timelines, or to exercise commercially reasonable efforts to develop and commercialize licensed products, in order to maintain the licenses. In spite of our efforts, our licensors might conclude that we have materially breached our obligations under such license agreements and might therefore terminate the license agreements, thereby removing or limiting our ability to develop and commercialize products and technology covered by these license agreements. If these in-licenses are terminated, or if the underlying patents fail to provide the intended exclusivity, competitors or other third parties would have the freedom to seek regulatory approval of, and to market, products identical to ours and we may be required to cease our development and commercialization of certain of our product candidates or of our current BBB platform technology. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and growth prospects.

Moreover, disputes may arise regarding intellectual property subject to a licensing agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- the sublicensing of patent and other rights under our collaborative development relationships;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- the inventorship and ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners; and
- the priority of invention of patented technology.

In addition, the agreements under which we currently license intellectual property or technology from third parties are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations and growth prospects. Moreover, if disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates, which could have a material adverse effect on our business, financial conditions, results of operations and growth prospects.

In addition, the United States federal government retains certain rights in inventions produced with its financial assistance under the Patent and Trademark Law Amendments Act, or the Bayh-Dole Act. The federal government retains a “nonexclusive, nontransferable, irrevocable, paid-up license” for its own benefit. The Bayh-Dole Act also provides federal agencies with “march-in rights.” March-in rights allow the government, in specified circumstances, to require the contractor or successors in title to the patent to grant a “nonexclusive, partially exclusive, or exclusive license” to a “responsible applicant or applicants.” If the patent owner refuses to do so, the government may grant the license itself. If, in the future, we co-own or license in technology which is critical to our business that is developed in whole or in part with federal funds subject to the Bayh-Dole Act, our ability to enforce or otherwise exploit patents covering such technology may be adversely affected.

We may not be able to protect our intellectual property and proprietary rights throughout the world.

Filing, prosecuting, and defending patents on our BBB platform technology, product candidates and other technologies in all countries throughout the world would be prohibitively expensive, and the laws of foreign countries may not protect our rights to the same extent as the laws of the United States. Further, our ability to pursue patents throughout the world may be delayed or affected due to the COVID-19 global pandemic. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. 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 have patent protection but enforcement is not as strong as that in the United States. These products may compete with our products, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from 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, trade secrets, and other intellectual property protection, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our intellectual property and proprietary rights

generally. European applications will soon have the option, upon grant of a patent, of becoming a Unitary Patent which will be subject to the jurisdiction of the Unitary Patent Court ("UPC"). This will be a significant change in European patent practice. As the UPC is a new court system, there is no precedent for the court, increasing the uncertainty. Proceedings to enforce our intellectual property and proprietary rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly, could put our patent applications at risk of not issuing, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property and proprietary rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Geopolitical actions in the United States and in foreign countries could increase the uncertainties and costs surrounding the prosecution or maintenance of our patent applications or those of any current or future licensors and the maintenance, enforcement or defense of our issued patents or those of any current or future licensors. For example, the United States and foreign government actions related to Russia's invasion of Ukraine may limit or prevent filing, prosecution, and maintenance of patent applications in Russia. Government actions may also prevent maintenance of issued patents in Russia. These actions could result in abandonment or lapse of our patents or patent applications, resulting in partial or complete loss of patent rights in Russia. If such an event were to occur, it could have a material adverse effect on our business. In addition, a decree was adopted by the Russian government in March 2022, allowing Russian companies and individuals to exploit inventions owned by patentees that have citizenship or nationality in, are registered in, or predominately have primary place of business or profit-making activities in the United States and other countries that Russia has deemed unfriendly without consent or compensation. Consequently, we may be unable to prevent third parties from practicing our inventions in Russia or from selling or importing products made using our inventions in and into Russia. Accordingly, our competitive position may be impaired, and our business, financial condition, results of operations and prospects may be adversely affected.

Many countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we or any of our licensors is forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired, and our business, financial condition, results of operations, and growth prospects may be adversely affected.

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

Periodic maintenance fees, renewal fees, annuity fees, and various other government fees on patents and applications will be due to be paid to the USPTO and various government patent agencies outside of the United States over the lifetime of our owned or licensed patents and applications. In certain circumstances, we rely on our licensing partners to pay these fees due to U.S. and non-U.S. patent agencies. The USPTO and various non-U.S. government agencies require compliance with several procedural, documentary, fee payment, and other similar provisions during the patent application process. We are also dependent on our licensors to take the necessary action to comply with these requirements with respect to our licensed intellectual property. In some cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. There are situations, however, in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in a partial or complete loss of patent rights in the relevant jurisdiction. In such an event, potential competitors might be able to enter the market with similar or identical products or technology, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

Geopolitical actions in the United States and in foreign countries could prevent us from continuing to make these periodic payments in certain locations. For example, the United States and foreign government actions related to Russia's invasion of Ukraine may limit our ability to make or prevent us from making these payments in Russia. These actions could result in abandonment or lapse of our patents or patent applications, resulting in partial or complete loss of patent rights in Russia, which could adversely affect our business.

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

Changes in either the patent laws or interpretation of the patent laws in the United States could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. Assuming that other requirements for patentability are met, prior to March 2013, in the United States, the first to invent the claimed invention was entitled to the patent, while outside the United States, the first to file a patent application was entitled to the patent. After March 2013, under the Leahy-Smith America Invents Act (the "America Invents Act"), enacted in September 2011, the United States transitioned to a first inventor to file system in which, assuming that other requirements for patentability are met, the first inventor to file a patent application will be entitled to the patent on an invention regardless of whether a third party was the first to invent the claimed invention. A third party that files a patent application in the USPTO after March 2013, but before us could therefore be awarded a patent covering an invention of ours even if we had made the invention before it was made by such third party. This will require us to be cognizant going forward of the time from invention to filing of a patent application. Since patent applications in the United States and most other countries are confidential for a period of time after filing or until issuance, we cannot be certain that we or

our licensors were the first to either (i) file any patent application related to our BBB platform technology, product candidates or other technologies or (ii) invent any of the inventions claimed in our or our licensor's patents or patent applications.

The America Invents Act also includes a number of significant changes that affect the way patent applications will be prosecuted and also may affect patent litigation. These include allowing third-party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent by USPTO administered post-grant proceedings, including post-grant review, *inter partes* review, and derivation proceedings. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in United States federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action. Therefore, the America Invents Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our owned or in-licensed patent applications and the enforcement or defense of our owned or in-licensed issued patents, all of which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

In addition, the patent positions of companies in the development and commercialization of biologics and pharmaceuticals are particularly uncertain. Recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. For example, the Supreme Court of the United States held in *Amgenv. Sanofi* (2023) that a functionally claimed genus was invalid for failing to comply with the enablement requirement of the Patent Act. In addition, the Federal circuit recently issued a decision involving the interaction of patent term adjustment (PTA), terminal disclaimers, and obvious-type double patenting. This combination of events has created uncertainty with respect to the validity and enforceability of patents, once obtained. Depending on future actions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could have a material adverse effect on our existing patent portfolio and our ability to protect and enforce our intellectual property in the future. For example, in *Assoc. for Molecular Pathology v. Myriad Genetics, Inc.* (2013), the U.S. Supreme Court held that certain claims to DNA molecules are not patentable. While we do not believe that any of the patents owned or licensed by us will be found invalid based on this decision, we cannot predict how future decisions by the courts, the U.S. Congress or the USPTO may impact the value of our patents.

Issued patents covering our BBB platform technology, product candidates and other technologies could be found invalid or unenforceable if challenged in court or before administrative bodies in the United States or abroad.

If we or one of our licensors initiated legal proceedings against a third party to enforce a patent covering our BBB platform technology, product candidates or other technologies, the defendant could counterclaim that such patent is invalid or unenforceable or raise a defense to infringement. In patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of subject matter eligibility for patenting, novelty, obviousness, or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. Grounds for defenses to infringement include statutory exemptions to patent infringement for uses related to submitting information to regulatory authorities to seek certain regulatory approvals. Third parties may raise claims challenging the validity or enforceability of our owned or in-licensed patents before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re-examination, post-grant review, *inter partes* review, interference proceedings, derivation proceedings, and equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings). Such proceedings could result in the revocation of, cancellation of, or amendment to our patents in such a way that they no longer cover our BBB platform technology, product candidates or other technologies. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, a judge or jury could find that our patent claims laws of nature or are otherwise ineligible for patenting, and we cannot be certain that there is no invalidating prior art, of which we or our licensing partners and the patent examiner were unaware during prosecution. If a third party were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our BBB platform technology, product candidates or other technologies. Such a loss of patent protection would have a material adverse impact on our business, financial condition, results of operations and growth prospects.
If

Patent terms may be inadequate to protect our competitive position on our product candidates for an adequate amount of time.

Patent rights are of limited duration. In the United States, if all maintenance fees are paid timely, the natural expiration of a patent is generally 20 years after its first effective filing date. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such product candidates are commercialized. Even if patents covering our product candidates are obtained, once the patent life has expired for a product, we do may be open to competition from biosimilar or generic products. As a result, our patent portfolio may not obtain provide us with sufficient rights to exclude others from commercializing product candidates similar or identical to ours. Upon issuance in the United States, the term of a patent can be increased by patent term extension and data exclusivity for any

product candidates we adjustment, which is based on certain delays caused by the USPTO, but this increase can be reduced or eliminated based on certain delays caused by the patent applicant during patent prosecution. The term of a United States patent may develop, our business may also be materially harmed.

Depending upon shortened if the timing, duration and specifics of any FDA marketing approval of any product candidates we may develop, one or more of our owned or in-licensed U.S. patents may be eligible for limited patent term extension under the Hatch-Waxman Act. The Hatch-Waxman Act permits a patent term extension of up to five years as compensation for patent term lost during the FDA regulatory review process. is terminally disclaimed over an earlier-filed patent. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent (PTE) based on regulatory delay may be extended and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. Similar extensions as compensation for patent term lost during regulatory review processes are also available in certain the United States. However, only a single patent can be extended for each marketing approval, and any patent can be extended only once, for a single product. Moreover, the scope of protection during the period of the PTE does not extend to the full scope of the claim, but instead only to the scope of the product as approved. Laws governing analogous PTEs in foreign countries and territories, such jurisdictions vary widely, as in Europe under do laws governing the ability to obtain multiple patents from a Supplementary Patent Certificate. However, single patent family. Additionally, we may not be granted receive an extension in the United States and/or foreign countries and territories because of, for example, failing if we fail to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing fail to apply prior to expiration of relevant patents or otherwise failing fail to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension PTE or restoration, or the term of any such extension is shorter less than what we request, the period during which we will have the right to exclusively market our product will be shortened and our competitors may obtain approval of competing products following our patent expiration and may take advantage of our business, financial condition, results of operations investment in development and growth prospects clinical trials by referencing our clinical and nonclinical data to launch their product earlier than might otherwise be the case, and our revenue could be materially harmed.

reduced, possibly materially.

We may be subject to claims challenging the inventorship of our patents and other intellectual property.

We or our licensors may be subject to claims that former employees, collaborators or other third parties have an interest in our owned or in-licensed patents, trade secrets, or other intellectual property as an inventor or co-inventor. For example, we or our licensors may have inventorship disputes arise from conflicting obligations of employees, consultants or others who are involved in developing our BBB platform technology, product candidates, or other technologies. Litigation may be necessary to defend against these and other claims challenging inventorship or our or our licensors' ownership of our owned or in-licensed patents, trade secrets, or other intellectual property. If we or our licensors fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, intellectual property that is important to our BBB platform technology, product candidates and other technologies. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations, and growth prospects.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to seeking patents for our BBB platform technology, product candidates and other technologies, we also rely on trade secrets and confidentiality agreements to protect our unpatented know-how, technology, and other proprietary information and to maintain our competitive position. Trade secrets and know-how can be difficult to protect. We expect our trade secrets and know-how to over time be disseminated within the industry through independent development, the publication of journal articles describing the methodology, and the movement of personnel from academic to industry scientific positions.

We seek to protect these trade secrets and other proprietary technology, in part, by entering into nondisclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, CROs, contract manufacturers, consultants, advisors, and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants as well as train our employees not to bring or use proprietary information or technology from former employers to us or in their work, and remind former employees when they leave their employment of their confidentiality obligations. We cannot guarantee that we have entered into such agreements with each party that may have or have had access to our trade secrets or proprietary technology and processes. Despite our efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive, and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor or other third party, we would have no right to prevent them from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor or other third party, our competitive position would be materially and adversely harmed.

We may not be successful in obtaining, through acquisitions, in-licenses or otherwise, necessary rights to our BBB platform technology, product candidates or other technologies.

We currently have rights to intellectual property, through licenses from third parties, to identify and develop our BBB platform technology and product candidates. Many pharmaceutical companies, biotechnology companies, and academic institutions are competing with us in the field fields of neurodegeneration neurodegenerative and lysosomal storage diseases and BBB technology and may have patents and have filed and are likely filing plan to file patent applications potentially relevant to our business. In order to avoid infringing these third-party patents, we may find it necessary or prudent to obtain licenses to such patents from such third-party intellectual property holders. We may also require licenses from third parties for certain BBB technologies that we are evaluating for use with our current or future product candidates. In addition, with respect to any patents we co-own with third parties, we may require licenses to such co-owners' interest to such patents. However, we may be unable to secure such licenses or otherwise acquire or in-license any compositions, methods of use, processes, or other intellectual property rights from third parties that we identify as necessary for our current or future product candidates and our BBB platform technology. The licensing or acquisition of third-party intellectual property rights is a competitive area, and several more established companies may pursue strategies to license or acquire third-party intellectual property rights that we may consider attractive or necessary. These established companies may have a competitive advantage over us due to their size, capital resources, and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment or at all. If we are unable to successfully obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon development of the relevant program or product candidate, which could have a material adverse effect on our business, financial condition, results of operations, and growth prospects.

We may be subject to claims that our employees, consultants, or advisors have wrongfully used or disclosed alleged trade secrets of their current or former employers or claims asserting ownership of what we regard as our own intellectual property.

Many of our employees, consultants, and advisors are currently or were previously employed at universities or other biotechnology or pharmaceutical companies, including our licensors, competitors, and potential competitors. Although we try to ensure that our employees, consultants, and advisors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these individuals have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such individual's current or former employer. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

In addition, while it is our policy to require our employees and contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own. The assignment of intellectual property rights may not be self-executing or the assignment agreements may be breached, and we may be forced to bring claims against third parties or defend claims that they may bring against us to determine the ownership of what we regard as our intellectual property. Such claims could have a material adverse effect on our business, financial condition, results of operations, and growth prospects.

Third-party claims of intellectual property infringement, misappropriation, or other violation against us, our licensors, or our collaborators may prevent or delay the development and commercialization of our BBB platform technology, product candidates, and other technologies.

The field fields of discovering treatments for neurodegenerative and lysosomal storage diseases, especially using BBB technology, is highly competitive and dynamic. Due to the focused research and development that is taking place by several companies, including us and our competitors, in this field, these fields, the intellectual property landscape is in flux, and it may remain uncertain in the future. As such, there may be significant intellectual property litigation and proceedings relating to our owned, and in-licensed, and other third-party intellectual property and proprietary rights in the future.

Our commercial success depends in part on our, our licensors' and our collaborators' ability to avoid infringing, misappropriating, and otherwise violating the patents and other intellectual property rights of third parties. There is a substantial amount of complex litigation involving patents and other intellectual property rights in the biotechnology and pharmaceutical industries, as well as administrative proceedings for challenging patents, including interference, derivation, and reexamination proceedings before the USPTO or oppositions and other comparable proceedings in foreign jurisdictions. As discussed above, recently, due to changes in U.S. law referred to as patent reform, new procedures including *inter partes* review and post-grant review have been implemented. As stated above, this reform adds uncertainty to the possibility of challenge to our patents in the future.

Numerous U.S. and foreign issued patents and pending patent applications owned by third parties exist relating to BBB technology and in the fields in which we are developing our product candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our BBB platform technology, product candidates, and other technologies may give rise to claims of infringement of the patent rights of others. We cannot assure you that our BBB platform technology, product

candidates, and other technologies that we have developed, are developing or may develop in the future will not infringe existing or future patents owned by third parties. We may not be aware of patents that have already been issued and that a third party, for example, a competitor in the fields in which we are developing our BBB platform technology, product candidates, and other technologies might assert are infringed by our current or future BBB platform technology, product candidates or other technologies, including claims to compositions, formulations, methods of manufacture or methods of use or treatment that cover our BBB platform technology, product candidates, or other technologies. It is also possible that patents owned by third parties of which we are aware, but which we do not believe are relevant to our BBB platform technology, product candidates, or other technologies, could be found to be infringed by our BBB platform technology, product candidates, or other technologies. In addition, because patent applications can take many years to issue, there may be currently pending patent applications that may later result in issued patents that our BBB platform technology, product candidates, or other technologies may infringe.

Third parties may have patents or obtain patents in the future and claim that the manufacture, use, or sale of our BBB platform technology, product candidates, or other technologies infringes upon these patents. In the event that any third-party claims that we infringe their patents or that we are otherwise employing their proprietary technology without authorization and initiates litigation against us, even if we believe such claims are without merit, a court of competent jurisdiction could hold that such patents are valid, enforceable, and infringed by our BBB platform technology, product candidates, or other technologies. In this case, the holders of such patents may be able to block our ability to commercialize the applicable product candidate or technology unless we obtain a license under the applicable patents, or until such patents expire or are finally determined to be held invalid or unenforceable. Such a license may not be available on commercially reasonable terms or at all. Even if we are able to obtain a license, the license would likely obligate us to pay license fees or royalties or both, and the rights granted to us might be nonexclusive, which could result in our competitors gaining access to the same intellectual property. If we are unable to obtain a necessary license to a third-party patent on commercially reasonable terms, we may be unable to commercialize our BBB platform technology, product candidates, or other technologies, or such commercialization efforts may be significantly delayed, which could in turn significantly harm our business.

Defense of infringement claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of management and other employee resources from our business, and may impact our reputation. In the event of a successful claim of infringement against us, we may be enjoined from further developing or commercializing our infringing BBB platform technology, product candidates, or other technologies. In addition, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, obtain one or more licenses from third parties, pay royalties, and/or redesign our infringing product candidates or technologies, which may be impossible or require substantial time and monetary expenditure. In that event, we would be unable to further develop and commercialize our BBB platform technology, product candidates, or other technologies, which could harm our business significantly.

Engaging in litigation to defend against third parties alleging that we have infringed, misappropriated, or otherwise violated their patents or other intellectual property rights is very expensive, particularly for a company of our size, and time-consuming. Some of our competitors may be able to sustain the costs of litigation or administrative proceedings more effectively than we can because of greater financial resources. Patent litigation and other proceedings may also absorb significant management time. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings against us could impair our ability to compete in the marketplace. The occurrence of any of the foregoing could have a material adverse effect on our business, financial condition, or results of operations or growth prospects.

We may become involved in lawsuits to protect or enforce our patents and other intellectual property rights, which could be expensive, time consuming, and unsuccessful.

Competitors may infringe our patents or the patents of our licensing partners, or we may be required to defend against claims of infringement. In addition, our patents or the patents of our licensing partners also may become involved in inventorship, priority, or validity disputes. To counter or defend against such claims can be expensive and time consuming. In an infringement proceeding, a court may decide that a patent in which we have an interest is invalid or unenforceable, the other party's use of our patented technology falls under the safe harbor to patent infringement under 35 U.S.C. §271(e)(1), or may refuse to stop the other party from using the technology at issue on the grounds that our owned and in-licensed patents do not cover the technology in question. An adverse result in any litigation proceeding could put one or more of our owned or in-licensed patents at risk of being invalidated or interpreted narrowly. 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.

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses and could distract our personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions, or other interim proceedings or developments, and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing, or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected.

Our registered or unregistered trademarks or trade names may be challenged, infringed, circumvented, or declared generic, or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential partners or customers in our markets of interest. At times, competitors or other third parties may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected. Our efforts to enforce or protect our proprietary rights related to trademarks, trade secrets, domain names, copyrights, or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely affect our business, financial condition, results of operations, and growth prospects.

Risks Related to Our Operations

We are highly dependent on our key personnel, and if we are not successful in attracting, motivating and retaining highly qualified personnel, we may not be able to successfully implement our business strategy.

Our ability to compete in the highly competitive biotechnology and pharmaceutical industries depends upon our ability to attract, motivate and retain highly qualified managerial, scientific, and medical personnel. We are highly dependent on our management, particularly our Chief Executive Officer, Dr. Ryan Watts, and our scientific and medical personnel. The loss of the services provided by any of our executive officers, other key employees, and other scientific and medical advisors, and our inability to find suitable replacements, could result in delays in the development of our product candidates and harm our business.

We primarily conduct our operations at our facility in South San Francisco, a region that is headquarters to many other biopharmaceutical companies and many academic and research institutions. Competition for skilled personnel is intense and the turnover rate can be high, which may limit our ability to hire and retain highly qualified personnel on acceptable terms or at all. We expect that we may need to recruit talent from outside of our region, and doing so may be costly and difficult. In response to increased competition in the labor market and rising inflation, we may need to adjust employee cash compensation or employee equity compensation.

To induce valuable employees to remain at our company, in addition to salary and cash incentives, we have provided restricted stock and stock option grants that vest over time. The value to employees of these equity grants that vest over time may be significantly affected by movements in our stock price that are beyond our control, and may at any time be insufficient to counteract more lucrative offers from other companies. Although we have employment agreements with our key employees, these employment agreements provide for at-will employment, which means that any of our employees could leave our employment at any time, with or without notice. We do not maintain “key man” insurance policies on the lives of all of these individuals or the lives of any of our other employees. If we are unable to attract and incentivize quality personnel on acceptable terms, or at all, it may cause our business and operating results to suffer.

We will need to grow the size and capabilities of our organization, and we may experience difficulties in managing this growth.

As of September 30, 2023 March 31, 2024, we had approximately 447 375 employees, all of whom were full-time. As our development plans and strategies develop, we must add a significant number of additional managerial, operational, financial, and other personnel. Future growth will impose significant added responsibilities on members of management, including recruiting, integrating, and retaining additional employees; managing our internal development efforts; and expanding our controls, reporting systems, and procedures.

Our future financial performance and our ability to continue to develop and, if approved, commercialize our product candidates will depend, in part, on our ability to effectively manage any future growth. Our management may also have to divert a disproportionate amount of its attention away from day-to-day activities in order to manage these growth activities.

We currently rely, and for the foreseeable future will continue to rely, in substantial part on certain independent organizations, advisors, and consultants to provide certain services. There can be no assurance that the services of these independent organizations, advisors, and consultants will continue to be available to us on a timely basis when needed, or that we can find qualified replacements. In addition, if we are unable to effectively manage our outsourced activities or if the quality or accuracy of the services provided by consultants is compromised for any reason, our clinical trials may be extended, delayed, or terminated, and we may not be able to obtain regulatory approval of our product candidates or otherwise advance our business. There can be no assurance that we will be able to manage our existing consultants or find other competent outside contractors and consultants on economically reasonable terms, if at all.

If we are not able to effectively manage our growth, we may not be able to successfully implement the tasks necessary to further develop our product candidates and, accordingly, may not achieve our research, development, and commercialization goals.

We have engaged in and may in the future engage in acquisitions or strategic partnerships, which may increase our capital requirements, dilute our stockholders, cause us to incur debt or assume contingent liabilities, and subject us to other risks.

We have in the past engaged in acquisitions and strategic partnerships, and we may engage in various acquisitions and strategic partnerships in the future, including licensing or acquiring complementary products, intellectual property rights, technologies, or businesses. businesses as part of our business strategy. For example, we have collaboration agreements with Takeda, Sanofi and Biogen, and issued stock in connection with entering into certain of those agreements in 2018 and 2020. Any acquisition or strategic partnership such transaction may entail numerous risks, including:

- increased operating expenses and cash requirements;
- the assumption of indebtedness or contingent liabilities;
- the issuance of our equity securities which would result in dilution to our stockholders;
- assimilation of operations, intellectual property, products and product candidates of an acquired company, including difficulties associated with integrating new personnel;
- the diversion of our management's attention from our existing product programs and initiatives in pursuing such an acquisition or strategic partnership;
- retention of key employees, the loss of key personnel, employees, and uncertainties in our ability to maintain key business relationships;
- risks and uncertainties associated with the other party to such a transaction, including the prospects of that party and their existing products or product candidates and regulatory approvals; and
- our inability to generate revenue from acquired intellectual property, technology and/or products sufficient to meet our objectives or offset the associated transaction and maintenance costs.

In addition, if we undertake such a transaction, 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 expense.

Our internal computer systems, or those used by our third-party research institution collaborators, CROs, or other contractors or consultants, may fail or suffer other breakdowns, cyberattacks, or information security breaches or incidents that could compromise the confidentiality, integrity, and availability of such systems and data, expose us to liability, and affect our reputation.

We are increasingly dependent upon information technology systems, infrastructure, and data to operate our business. We also rely on third-party vendors and their information technology systems. Despite the implementation of security measures, our internal computer systems and those of our collaborators, CROs, and other contractors and consultants may be vulnerable to damage, outages and interruptions resulting from computer viruses and other malicious code or unauthorized access, or breached, compromised, or otherwise subject to security incidents due to operator error, malfeasance, or other system disruptions. Geopolitical events, such as war and armed conflicts, may increase the risks of cyber-attacks, disruptions, and security breaches and incidents that we and these third parties face. As the cyber-threat landscape evolves, attacks are growing in frequency, sophistication, and intensity, and are becoming increasingly difficult to detect. Security threats can come from a variety of sources, ranging in sophistication from an individual hacker to a state-sponsored attack. Cyber threats may be broad-based or otherwise generic in nature, or they may be custom-crafted against our information systems or those of our collaborators, CROs, or other contractors or consultants.

Over the past few years, cyber-attacks have become more prevalent, intense, sophisticated, and much harder to detect and defend against. Such attacks could include the use of key loggers or other harmful and virulent malware, including ransomware or other denials of service, and can be deployed through malicious websites, the use of social engineering and/or other means. We and our collaborators, CROs, or other contractors and consultants may not be able to anticipate all types of security threats, and we may not be able to implement preventive measures effective against all such security threats. The techniques used by cyber criminals change frequently, may not be recognized until launched, and can originate from a wide variety of sources. Although to our knowledge we have not experienced any such material system failure or security breach or incident to date, if a breakdown, cyberattack or other information security breach or incident were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs and our business operations, whether due to loss or misappropriation of trade secrets or loss of, or unauthorized modification, unavailability, disclosure, or other unauthorized processing of other proprietary information or other similar disruption and we could incur liability and reputational damage. For example, any corruption, loss, or other unavailability of clinical trial data from completed, ongoing or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Likewise, we rely on our third-party research institution collaborators for research and development of our product candidates and other third

parties for the manufacture of our product candidates and to conduct clinical trials, and similar events relating to their computer systems could also have a material adverse effect on our business.

Cyber-attacks, breaches, interruptions, or other data security incidents could result in legal claims or proceedings by private parties or governmental authorities, liability under federal or state laws that protect the privacy of personal information, regulatory penalties, significant remediation costs, disrupt key business operations, and divert attention of management and key information technology resources. In the United States, notice of breaches must be made to affected individuals, the U.S. Secretary of the Department of Health and Human Services ("HHS"), and for extensive breaches, notice may need to be made to the media or U.S. state attorneys general. Such a notice could harm our reputation and our ability to compete. In addition, U.S. state attorneys general are authorized to bring civil actions seeking either injunctions or damages in response to violations that threaten the privacy of state residents. There can be no assurance that we, our collaborators, CROs, contractors, consultants, and any other business counterparties will be successful in efforts to detect, prevent, protect against, or fully recover systems or data from all break-downs, service interruptions, attacks, or security breaches or incidents. Although we maintain standalone cybersecurity insurance, the costs related to significant security breaches, incidents, or disruptions could be material and exceed the limits of any insurance coverage we have, and may result in increases in our insurance costs. Relevant insurance may in the future become unavailable to us on commercially reasonable terms or at all. Any disruption or security breach or incident that results in or is perceived to have resulted in a loss of, or damage to, our data or systems, or inappropriate disclosure, use, acquisition, transfer, modification, unavailability, or other processing of confidential or proprietary information, including data related to our personnel, could result in the loss, unauthorized modification, use, unavailability, disclosure or other unauthorized processing of critical or sensitive date, data, and could cause us to incur liability. Further, in any such event, the development and commercialization of our product candidates could be delayed and our business and operations could be adversely affected. Any of the foregoing could result in financial, legal, business, or reputational harm to us.

Business disruptions could seriously harm our future revenue and financial condition and increase our costs and expenses.

Our operations, and those of our third-party research institution collaborators, CROs, CDMOs, suppliers, and other contractors and consultants, could be subject to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, health epidemics such as COVID-19, and other natural or man-made disasters or business interruptions, for which we are partly uninsured. In addition, we rely on our third-party research institution collaborators for conducting research and development of our product candidates, and they may be affected by bank failures or instability in the financial services sector, government shutdowns, or withdrawn funding. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses. We rely on third-party manufacturers to produce and process our product candidates. Our ability to obtain clinical supplies of our product candidates could be disrupted if the operations of these suppliers are affected by a man-made or natural disaster or other business interruption.

The majority of our operations including our corporate headquarters are located in a single facility in South San Francisco, California. California and Salt Lake City, Utah. Damage or extended periods of interruption to our corporate, development or research facilities due to fire, extreme weather conditions or natural disaster, power loss, communications failure, unauthorized entry, or other events could cause us to cease or delay development of some or all of our product candidates. Although we maintain property damage and business interruption insurance coverage on these facilities, our insurance might not cover all losses under such circumstances and our business may be seriously harmed by such delays and interruption.

Our business is subject to economic, political, regulatory and other risks associated with international operations.

Our business is subject to risks associated with conducting business internationally. Some In addition to a subsidiary located in Zurich, Switzerland, some of our suppliers and collaborative relationships are located outside the United States. Accordingly, our future results could be harmed by a variety of factors, including:

- economic weakness, including inflation, rising interest rates or political instability in certain non-U.S. economies and markets;
- differing and changing regulatory requirements in non-U.S. countries;
- challenges enforcing our contractual and intellectual property rights, especially in those non-U.S. countries that do not offer the same level of intellectual property protection as the United States;
- difficulties in compliance with non-U.S. laws and regulations;
- changes in non-U.S. regulations and customs, tariffs, and trade barriers;
- changes in non-U.S. currency exchange rates and currency controls;
- changes in a specific country's or region's political or economic environment;

- trade protection measures, import or export licensing requirements, or other restrictive government actions;
- negative consequences from changes in tax laws;
- compliance with tax, employment, immigration, and labor laws for employees living or traveling abroad;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- difficulties associated with staffing and managing international operations, including differing labor relations;
- potential liability under the FCPA, UK Bribery Act, or comparable foreign laws;
- business interruptions resulting from geopolitical actions, including war such as Russia's invasion of Ukraine, and armed conflict, terrorism, natural disasters including earthquakes, typhoons, floods, and fires, or health epidemics such as COVID-19; epidemics; and
- cyberattacks, which are growing in frequency, sophistication and intensity, and are becoming increasingly difficult to detect.

In particular, there is currently significant uncertainty about the future relationship between the United States and various other countries, most significantly China, with respect to trade policies, treaties, tariffs, taxes, and other limitations on cross-border operations. The U.S. government has and continues to make significant additional changes in U.S. trade policy and may continue to take future actions that could negatively impact U.S. trade. For example, legislation has been introduced in Congress to limit certain U.S. biotechnology companies from using equipment or services produced or provided by select Chinese biotechnology companies, and others in Congress have advocated for the use of existing executive branch authorities to limit those Chinese service providers' ability to engage in business in the U.S. We cannot predict what actions may ultimately be taken with respect to trade relations between the United States and China or other countries, what products and services may be subject to such actions or what actions may be taken by the other countries in retaliation. If we are unable to obtain or use services from existing service providers or become unable to export or sell our products to any of our customers or service providers, our business, liquidity, financial condition, and/or results of operations would be materially and adversely affected.

These and other risks associated with our planned international operations may materially adversely affect our ability to attain profitable operations.

Our ability to use our net operating loss carryforwards and certain other tax attributes may be limited.

As of December 31, 2022 December 31, 2023, we had federal net operating loss carryforwards of approximately $231.9 million $290.6 million, federal research and development tax credit carryforwards of approximately $42.6 million $53.1 million, and orphan tax credit carryforwards of approximately $19.7 million $37.4 million, some of which will begin to expire in 2035. 2034. Under Sections 382 and 383 of the United States Internal Revenue Code of 1986, as amended, (the "Code"), if a corporation undergoes an "ownership change" (generally defined as a greater than 50-percentage-point cumulative change (by value) in the equity ownership of certain stockholders over a rolling three-year period), the corporation's ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes to offset its post-change taxable income or taxes may be limited. We have experienced ownership changes in the past, and we may also experience ownership changes in the future as a result of subsequent shifts in our stock ownership, including in connection with our October 2022 offering, some of which are outside our control. As a result, our ability to use our pre-change net operating loss carryforwards and other pre-change tax attributes to offset post-change taxable income or taxes may be subject to limitation.

We may be subject to adverse legislative or regulatory tax changes that could negatively impact our financial condition.

The rules dealing with U.S. federal, state and local income taxation are constantly under review by legislators and by the IRS and the U.S. Treasury Department. Changes to tax laws (which changes may have retroactive application) have occurred and are likely to continue to occur in the future, which could adversely affect our shareholders. For example, in August 2022, the United States enacted the Inflation Reduction Act, which implemented a 15% minimum tax on book income for certain companies and introduced a 1% excise tax on stock buybacks. In addition, the current tax administration has proposed changes to the orphan drug tax credit. Changes in tax laws, regulation, or enforcement could adversely affect our stockholders or require us to implement changes to minimize increases in our tax liability.

Risks Related to Ownership of Our Common Stock

The market price of our common stock has been and may continue to be volatile, which could result in substantial losses for investors.

The trading price of our common stock has been and may continue to be highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control. In addition to the factors discussed in this "Risk Factors" section and elsewhere in this report, these factors include:

- the success of existing or new competitive products or technologies;
- the timing and results of clinical trials for our current product candidates and any future product candidates that we may develop;
- commencement or termination of collaborations for our product development and research programs;
- failure to achieve development, regulatory, or commercialization milestones under our collaborations;
- failure or discontinuation of any of our product development and research programs;
- failure to develop our BBB platform technology;
- results of preclinical studies, clinical trials, or regulatory approvals of product candidates of our competitors, or announcements about new research programs or product candidates of our competitors;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents, or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our research programs, clinical development programs, or product candidates that we may develop;
- the results of our efforts to develop additional product candidates or products;
- actual or anticipated changes in estimates as to financial results, development timelines, or recommendations by securities analysts;
- announcement or expectation of additional financing efforts;
- sales of our common stock by us, our insiders, or other stockholders;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in the structure of healthcare payment systems or in accounting standards;
- ineffectiveness of our internal controls;
- significant lawsuits, including patent or stockholder litigation;
- market conditions in the pharmaceutical and biotechnology sectors; and
- other events or factors affecting general economic, industry, and market conditions, including bank failures or instability in the financial services sector, geopolitical events such as Russia's invasion of Ukraine war and armed conflict, and outbreaks of pandemic diseases such as COVID-19.

In recent years, the stock market in general, and the market for pharmaceutical and biotechnology companies in particular, has experienced significant price and volume fluctuations that have often been unrelated or disproportionate to changes in the operating performance of the companies whose stock is experiencing those price and volume fluctuations. Broad market and industry factors may seriously affect the market price of our common stock, regardless of our actual operating performance. In the past, when the market price of a stock has been volatile, holders of that stock have instituted securities class action litigation against the company that issued the stock. If any of our stockholders

were to bring a lawsuit against us, the defense and disposition of any such lawsuits could be costly and divert the time and attention of our management and harm our operating results, regardless of the merits of such a claim.

If securities analysts publish negative evaluations of our stock, or if they do not publish research or reports about our business, the price of our stock and trading volume could decline.

The trading market for our common stock relies in part on the research and reports that industry or financial analysts publish about us or our business. If one or more of the analysts covering our business downgrade their evaluations of our stock, or if we fail to meet the expectations of analysts, the price of our stock could decline. If one or more of these analysts cease to cover our stock, we could lose visibility in the market for our stock, which in turn could cause our stock price or trading volume to decline.

Sales of substantial amounts of our common stock in the public markets, or the perception that such sales might occur, could cause the market price of our common stock to decline significantly, even if our business is doing well.

Sales of a substantial number of shares of our common stock in the public market, or the perception that these sales might occur, could depress the market price of our common stock and could impair our ability to raise capital through the sale of additional equity securities. We are unable to predict the effect that sales may have on the prevailing market price of our common stock.

Sales of our common stock by current stockholders may make it more difficult for us to sell equity or equity-related securities in the future at a time and price that we deem reasonable or appropriate, and make it more difficult for you to sell shares of our common stock.

Certain holders of shares of our common stock have rights, subject to conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. For example, on February 27, 2024, we entered into a Purchase Agreement with certain existing accredited investors in connection with a PIPE financing. Pursuant to this Purchase Agreement, we entered into an agreement granting an investor certain registration rights following such time that the investor may be deemed an affiliate of the Company. Any sales of securities by these stockholders, or the perception that sales will be made in the public market, could have a material adverse effect on the market price for our common stock.

We have registered on Form S-8 all shares of common stock that are issuable under our 2017 Equity Incentive Plan and 2017 Employee Stock Purchase Plan. As a consequence, these shares can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates.

Raising additional capital may cause dilution to our existing stockholders, restrict our operations, or require us to relinquish rights to our technologies or product candidates.

We may seek additional capital through a combination of public and private equity offerings, debt financings, strategic partnerships and alliances, and licensing arrangements. For example, in August 2020, we entered into the Provisional Biogen Collaboration Agreement, and in connection therewith issued and sold 13,310,243 shares of our common stock to Biogen in September 2020 for an aggregate purchase price of $465.0 million. We, and indirectly, our stockholders, will bear the cost of issuing and servicing all such securities. Additionally, collaborations we enter into with third parties may provide capital in the near term but limit our potential cash flow and revenue in the future. If we raise additional funds through strategic partnerships and alliances and licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies or product candidates, or grant licenses on terms unfavorable to us.

In January 2020, we sold 9.0 million shares of common stock in an underwritten follow-on offering pursuant to a shelf registration statement filed in March 2019 and, in October 2022, we sold 11.9 million 11.9 million shares of common stock in an underwritten public offering pursuant to a second shelf registration statement filed in February 2022. Also in February 2022, we entered into an equity distribution agreement with Goldman Sachs & Co. LLC, SVB Securities LLC, and Cantor Fitzgerald & Co., as sales agents, to establish an at-the-market facility pursuant to which we may offer and sell from time to time up to $400.0 million in shares of our common stock. On February 27, 2024, we announced a PIPE financing in which we sold 3,244,689 shares of our common stock and pre-funded warrants to purchase 26,046,065 shares of our common stock, resulting in gross proceeds of approximately $499.7 million.

Our decision to issue debt or equity securities in any future offering will depend on market conditions and other factors beyond our control, and therefore we cannot predict or estimate the amount, timing, or nature of any future offerings. To the extent that we raise additional capital through the sale of equity or debt securities, your ownership interest will be diluted, and the terms may include liquidation or other preferences that adversely affect your rights as a stockholder. The incurrence of indebtedness would result in increased fixed payment obligations and could involve restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell, or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. In addition, any sales of our common stock or other securities under our shelf registration statement could put downward pressure on our stock price. Additionally, collaborations we enter into with third parties may provide capital in

the near term but limit our potential cash flow and revenue in the future. If we raise additional funds through strategic partnerships and alliances and licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies or product candidates, or grant licenses on terms unfavorable to us.

Our principal stockholders and management own a significant percentage of our stock and will be able to exercise significant influence over matters subject to stockholder approval.

Our directors, executive officers, holders of more than 5% of our outstanding stock, and their respective affiliates beneficially own a significant percentage of our outstanding common stock. As a result, these stockholders, if they act together, may significantly influence all matters requiring stockholder approval, including the election of directors and approval of significant corporate transactions. This concentration of ownership may have the effect of delaying or preventing a change in control of our company that our other stockholders may believe is in their best interests. This in turn could have a material adverse effect on our stock price and may prevent attempts by our stockholders to replace or remove the board of directors or management.

If we are unable to maintain effective internal controls, our business, financial position and results of operations and growth prospects could be adversely affected.

As a public company, we are subject to reporting and other obligations under the Securities Exchange Act of 1934, as amended, ("Exchange Act"), including the requirements of Section 404 of the Sarbanes-Oxley Act, which require annual management assessments of the effectiveness of our internal control over financial reporting.

The rules governing the standards that must be met for management and our auditors to assess our internal control over financial reporting are complex and require significant documentation, testing, and possible remediation to meet the detailed standards under the rules. During the course of its testing, our management or auditors may identify material weaknesses or deficiencies which may not be remedied in time to meet the deadline imposed by the Sarbanes-Oxley Act. These reporting and other obligations place significant demands on our management and administrative and operational resources, including accounting resources.

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Our internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with U.S. GAAP. Any failure to maintain effective internal controls could have an adverse effect on our business, financial position, results of operations, and growth prospects.

Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud.

We are subject to the periodic reporting requirements of the Exchange Act. We designed our disclosure controls and procedures to reasonably assure that information we must disclose in reports we file or submit under the Exchange Act is accumulated and communicated to management, and recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures or internal controls and procedures, no matter how well-conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met.

These inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements due to error or fraud may occur and not be detected.

We do not expect to pay any dividends for the foreseeable future. Investors may never obtain a return on their investment.

We have never paid cash dividends on our common stock and do not anticipate that we will pay any dividends in the foreseeable future. We currently intend to retain our future earnings, if any, to maintain and expand our existing operations. If we do not pay dividends, our common stock may be less valuable because a return on your investment will only occur if our stock price appreciates, which may never occur.

Delaware law and provisions in our charter documents might discourage, delay, or prevent a change in control of our company or changes in our management and, therefore, depress the trading price of our common stock.

Provisions in our amended and restated certificate of incorporation and amended and restated bylaws may discourage, delay, or prevent a merger, acquisition, or other change in control that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares of our common stock. These provisions may also prevent or frustrate attempts by our stockholders to replace or remove our management. Therefore, these provisions could adversely affect the price of our common stock. Among other things, our charter documents:

- establish that our board of directors is divided into three classes, Class I, Class II, and Class III, with each class serving staggered three-year terms;
- provide that vacancies on our board of directors may be filled only by a majority of directors then in office, even though less than a quorum;
- provide that our directors may only be removed for cause;
- eliminate cumulative voting in the election of directors;
- authorize our board of directors to issues shares of preferred stock and determine the price and other terms of those shares, including preferences and voting rights, without stockholder approval;
- provide our board of directors with the exclusive right to elect a director to fill a vacancy or newly created directorship;
- permit stockholders to only take actions at a duly called annual or special meeting and not by written consent;
- prohibit stockholders from calling a special meeting of stockholders;
- require that stockholders give advance notice to nominate directors or submit proposals for consideration at stockholder meetings;
- authorize our board of directors, by a majority vote, to amend the bylaws; and
- require the affirmative vote of at least 66 2/3% or more of the outstanding shares of common stock to amend many of the provisions described above.

In addition, Section 203 of the General Corporation Law of the State of Delaware, (the "DGCL"), prohibits a publicly-held Delaware corporation from engaging in a business combination with an interested stockholder, generally a person which together with its affiliates owns, or within the last three years has owned, 15.0% of our voting stock, for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is approved in a prescribed manner.

Any provision of our amended and restated certificate of incorporation, amended and restated bylaws, or Delaware law that has the effect of delaying or preventing a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our common stock and could also affect the price that some investors are willing to pay for our common stock.

Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware and the federal district courts of the United States of America will be the exclusive forums for substantially all disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers, or employees.

Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware is the exclusive forum for:

- any derivative action or proceeding brought on our behalf;
- any action asserting a claim of breach of fiduciary duty;
- any action asserting a claim against us arising under the DGCL, our amended and restated certificate of incorporation, or our amended and restated bylaws; and
- any action asserting a claim against us that is governed by the internal-affairs doctrine.

Our amended and restated certificate of incorporation further provides that the federal district courts of the United States of America will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act.

These exclusive-forum provisions may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers, or other employees, which may discourage lawsuits against us and our directors, officers, and other employees. If a court were to find either exclusive-forum provision in our amended and restated certificate of incorporation to be inapplicable or unenforceable in an action or we do not enforce such provision, we may incur additional costs associated with resolving the dispute in other jurisdictions, which could seriously harm our business.

ITEM 2. UNREGISTERED SALES OF EQUITY SECURITIES AND USE OF PROCEEDS

Recent Sales of Unregistered Securities

None.On February 27, 2024, we entered into a Purchase Agreement with certain existing accredited investors for the private placement of (i) 3,244,689 shares of our common stock at a price of $17.07 per share and (ii) Pre-Funded Warrants to purchase an aggregate of 26,046,065 shares of our common stock at a purchase price of $17.06 per Pre-Funded Warrant, resulting in net proceeds of approximately $499.3 million. The Pre-Funded Warrants are exercisable at an exercise price of $0.01 and will be exercisable until exercised in full. The holders of Pre-Funded Warrants may not exercise a Pre-Funded Warrant if the holder, together with its affiliates, would beneficially own more than 4.99% of the number of shares of common stock outstanding immediately after giving effect to such exercise. The holders of Pre-Funded Warrants may increase or decrease such percentage not in excess of 19.99%, in the case of an increase, by providing at least 61 days' prior notice to the Company. The private placement closed on February 29, 2024, subject to customary closing conditions. We intend to use the net proceeds from the private placement to support our ongoing research and development activities, the acceleration and expansion of our proprietary BBB-crossing TV technology, as well as general corporate purposes and working capital. We filed a registration statement on March 22, 2024 for purposes of registering the shares of common stock sold in the private placement (including the shares of common stock underlying the Pre-Funded Warrants). We also granted a certain investor certain director nomination and additional registration rights, subject to certain exceptions, conditions, and limitations.

We are relying on the exemptions from registration available under Section 4(a)(2) and/or Rule 506(b) of Regulation D promulgated under the Securities Act with respect to transactions by an issuer not involving any public offering, and we filed a Form D with respect to the private placement.

Use of Proceeds from Registered Securities

In October 2022, we sold 11.9 million 11.9 million shares of common stock (inclusive of shares sold pursuant to an overallotment option granted to the underwriters in connection with the offering) through an underwritten public offering at a price of $26.50 per share for aggregate net proceeds of approximately $296.2 million. $296.2 million.

There have been no material changes in the planned use of the net proceeds from the follow-on public offering as described in the final prospectus supplement filed with the SEC on October 20, 2022. We have invested the funds received in short to intermediate term, interest-bearing investment-grade securities and government securities.

Issuer Purchases of Equity Securities

Not applicable.

ITEM 3. DEFAULTS UPON SENIOR SECURITIES

Not applicable.

ITEM 4. MINE SAFETY DISCLOSURES

Not applicable.

ITEM 5. OTHER INFORMATION

Securities Trading Plans of Directors and Executive Officers

Our policy governing transactions in our securities by our directors, officers, and employees permits our officers, directors and employees to enter into trading plans complying with Rule 10b5-1 under the Securities Exchange Act of 1934, as amended. As disclosed in the table below, during the third first quarter of 2023, 2024, certain of our executive officers and directors adopted a "Rule 10b5-1 trading arrangement". These plans provide for the sale of our common stock and are intended to satisfy the affirmative defense in Rule 10b5-1(c).

Name	Position	Date of Plan Adoption	Scheduled End Date of Trading Arrangement[1]	Maximum Total Shares of Common Stock to be Sold Under the Plan[2]
Ryan Watts, Ph.D. Vicki Sato	Director Chief Executive Officer	9/29/2023 3/21/2024	2/16/ 7/1/2025	300,000 30,720
Jennifer Cook	Director			
Alexander Schuth, M.D.	Chief Operating and Financial Officer	9/29/2023 3/1/2024	2/14/ 6/3/2025	116,918 1,458
Carole Ho, M.D.	Chief Medical Officer	9/29/2023	12/29/2024	340,953

(1) In each case, the trading arrangement may expire on an earlier date if and when all transactions under the arrangement are completed.

(2) These amounts represent This amount represents the maximum total shares that could be sold under the plan, but the amounts may change for executive officers due to the sale of shares to satisfy tax withholding requirements.

No other officers or directors, as defined in Rule 16a-1(f), adopted and/or terminated of a “Rule 10b5-1 trading arrangement” or a “non-Rule 10b5-1 trading arrangement,” as defined in Regulation S-K Item 408, during the third first quarter ended September 30, 2023 March 31, 2024.

ITEM 6. EXHIBITS

EXHIBIT INDEX

Exhibit Number	Description	Incorporated by Reference			
		Form	File No.	Number	Filing Date
4.1#	Form ofPre-FundedWarrant	—	—	—	
31.1	Certification of Chief Executive Officer pursuant to Section 302 of the Sarbanes-Oxley Act.	—	—	—	Filed herewith
31.2	Certification of Chief Financial Officer pursuant to Section 302 of the Sarbanes-Oxley Act.	—	—	—	Filed herewith
32.1*	Certification of Chief Executive Officer pursuant to Section 906 of the Sarbanes-Oxley Act.	—	—	—	Furnished herewith
32.2*	Certification of Chief Financial Officer pursuant to Section 906 of the Sarbanes-Oxley Act.	—	—	—	Furnished herewith
10.1#	Amendment to Definitive LRRK2 Agreement and Waiver of and Amendment to Right of First Negotiation, Option, and License Agreement.	—	—	—	Filed herewith
101.INS	XBRL Instance Document - the instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Incline XBRL document	—	—	—	Furnished herewith
101.SCH	Inline XBRL Taxonomy Extension Schema Document.	—	—	—	Furnished herewith
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document.	—	—	—	Furnished herewith
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document.	—	—	—	Furnished herewith
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document.	—	—	—	Furnished herewith
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document.	—	—	—	Furnished herewith
104	The cover page from the Company's Quarterly Report on Form 10-Q for the three months ended September 30, 2023 March 31, 2024, formatted in Inline XBRL (contained in Exhibit 101)	—	—	—	Furnished herewith

* The certifications attached as Exhibits 32.1 and 32.2 that accompany this Quarterly Report on Form 10-Q are not deemed filed with the Securities and Exchange Commission and are not to be incorporated by reference into any filing of Denali Therapeutics Inc. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, whether made before or after the date of this Quarterly Report on Form 10-Q, irrespective of any general incorporation language contained in such filing.

Certain information Portions of this exhibit have been omitted pursuant to a request for confidential treatment and this exhibit has been excluded from this exhibit because it is both not material and would likely cause competitive harm to filed separately with the registrant if publicly disclosed. Omissions are designated as [***]. SEC.

SIGNATURES

Pursuant to the requirements 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.

DENALI THERAPEUTICS INC.

Date: November May 7, 2023 2024

By: /s/ Ryan J. Watts

Ryan J. Watts, Ph.D.

President and Chief Executive Officer

(Principal Executive Officer)

Date: November May 7, 2023 2024

By: /s/ Alexander O. Schuth

Alexander O. Schuth, M.D.

Chief Operating and Financial Officer

(Principal Financial and Accounting Officer)

Exhibit 10.1 4.1

THESE SECURITIES REPRESENTED HEREBY AND THE SECURITIES ISSUABLE UPON EXERCISE OF THESE SECURITIES HAVE NOT BEEN REGISTERED WITH THE SECURITIES AND EXCHANGE COMMISSION OR THE SECURITIES COMMISSION OF ANY STATE BUT HAVE BEEN OR WILL BE ISSUED IN RELIANCE UPON AN EXEMPTION FROM REGISTRATION UNDER THE SECURITIES ACT OF 1933, AS AMENDED, AND, ACCORDINGLY, MAY NOT BE TRANSFERRED UNLESS (i) SUCH SECURITIES HAVE BEEN REGISTERED FOR SALE PURSUANT TO THE SECURITIES ACT OF 1933, AS AMENDED, (ii) SUCH SECURITIES MAY BE SOLD PURSUANT TO RULE 144, (ii) THE COMPANY HAS RECEIVED AN OPINION OF COUNSEL REASONABLY SATISFACTORY TO IT THAT SUCH TRANSFER MAY LAWFULLY BE MADE WITHOUT REGISTRATION UNDER THE SECURITIES ACT OF 1933, AS AMENDED, OR (iv) THE SECURITIES ARE TRANSFERRED WITHOUT CONSIDERATION TO AN AFFILIATE OF SUCH HOLDER OR A CUSTODIAL NOMINEE (WHICH FOR THE AVOIDANCE OF DOUBT SHALL REQUIRE NEITHER CONSENT NOR THE DELIVERY OF AN OPINION).

Amendment

FORM OF PRE-FUNDED WARRANT TO PURCHASE COMMON STOCK

Number of Shares: [ ]
(subject to

Definitive LRRK2 Agreement
and Waiver of and Amendment to
Right of First Negotiation, Option, and License Agreement adjustment)

Warrant No. Original Issue Date: [ ], 2024

Reference is hereby made to the Definitive LRRK2 Collaboration and License Agreement, entered into as of October 4, 2020 (the "LRRK2 Agreement"), by and between Denali Therapeutics Inc., a Delaware corporation (the "**Company**"), hereby certifies that, for good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, [ ] or its registered assigns (the "**Holder**"), is entitled, subject to the terms set forth below, to purchase from the Company up to a total of [ ] shares of common stock, $0.01 par value per share (the "**Common Stock**"), of the Company (each such share, a "**Warrant Share**" and all such shares, the "**Warrant Shares**") at an exercise price per share equal to $0.01 per share (as adjusted from time to time as provided in Section 9 herein, the "**Exercise Price**"), upon surrender of this Warrant to Purchase Common Stock (including any Warrants to Purchase Common Stock issued in exchange, transfer or replacement hereof, the "**Warrant**") at any time and from time to time on or after the date hereof (the "**Original Issue Date**"), subject to the following terms and conditions:

1. *Definitions*. For purposes of this Warrant, the following terms shall have the following meanings:

(a) "**Affiliate**" means with respect to any Person, any other Person directly or indirectly controlled by, controlling or under common control with, such Person, but only for so long as such control shall continue. For purposes of this definition, "control" (including, with correlative meanings, "controlled by", "controlling" and "under common control with") means, with respect to a Person, possession, direct or indirect, of (i) the power to direct or cause direction of the management and policies of such Person (whether through ownership of securities or partnership or other ownership interests, by contract or otherwise), or (ii) at least 50% of the voting securities (whether directly or pursuant to any option, warrant or other similar arrangement) or other comparable equity interests.

(b) "**Attribution Parties**" means, collectively, the following Persons and entities: (i) any direct or indirect Affiliates of the Holder, (ii) any Person acting or who could be deemed to be acting as a Group together with the Holder or any Attribution Parties and (iii) any other Persons whose beneficial ownership of the Company's Common Stock would or could

be aggregated with the Holder's and/or any other Attribution Parties for purposes of Section 13(d) or Section 16 of the Exchange Act. For clarity, the purpose of the foregoing is to subject collectively the Holder and all other Attribution Parties to the Maximum Percentage.

(c) "**Closing Sale Price**" means, for any security as of any date, the last trade price for such security on the Principal Trading Market for such security, as reported by Bloomberg Financial Markets, or, if such Principal Trading Market begins to operate on an extended hours basis and does not designate the last trade price, then the last trade price of such security prior to 4:00 P.M., New York City time, as reported by Bloomberg Financial Markets, or if the foregoing do not apply, the last trade price of such security in the over-the-counter market on the electronic bulletin board for such security as reported by Bloomberg Financial Markets. If the Closing Sale Price cannot be calculated for a security on a particular date on any of the foregoing bases, the Closing Sale Price of such security on such date shall be the fair market value as mutually determined by the Company and the Holder. If the Company and the Holder are unable to agree upon the fair market value of such security, then the Board of Directors of the Company shall use its good faith judgment to determine the fair market value. The Board of Directors' determination shall be binding upon all parties absent demonstrable error. All such determinations shall be appropriately adjusted for any stock dividend, stock split, stock combination or other similar transaction during the applicable calculation period.

(d) "**Commission**" means the United States Securities and Exchange Commission.

(e) "**Exchange Act**" means the Securities Exchange Act of 1934, as amended.

(f) "**Group**" shall have the meaning ascribed to it in Section 13(d) of the Exchange Act, and all related rules, regulations and jurisprudence.

(g) "**Person**" means an individual, a limited liability company, a partnership, a joint venture, a corporation, a trust, an unincorporated organization, any other entity and a government or any department or agency thereof.

(h) "**Principal Trading Market**" means the national securities exchange or other trading market on which the Common Stock is primarily listed on and quoted for trading, which, as of the Original Issue Date, shall be the Nasdaq Global Select Market.

(i) "**Securities Act**" means the Securities Act of 1933, as amended.

(j) "**Standard Settlement Period**" means the standard settlement period, expressed in a number of Trading Days, for the Principal Trading Market with respect to the Common Stock that is in effect on the date of delivery of an applicable Exercise Notice, which as of the Original Issue Date was "T+2."

(k) "**Trading Day**" means any weekday on which the Principal Trading Market is normally open for trading.

(l) "**Transfer Agent**" means Broadridge Financial Solutions, Inc., the Company's transfer agent and registrar for the Common Stock, and any successor appointed in such capacity.

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2. *Registration of Warrants*. The Company shall register ownership of this Warrant, upon records to be maintained by the Company for that purpose (the "**Warrant Register**"), in the name of the record Holder (which shall include the initial Holder or, as the case may be, any assignee to which this Warrant is permissibly assigned hereunder) from time to time. The Company may deem and treat the registered Holder of this Warrant as the absolute owner hereof for the purpose of any exercise hereof or any distribution to the Holder, and for all other purposes, absent actual notice to the contrary.

3. *Registration of Transfers*. Subject to compliance with all applicable securities laws, the Company shall, or will cause its Transfer Agent to, register the transfer of all or any portion of this Warrant in the Warrant Register, upon surrender of this Warrant, together with a written assignment of this Warrant substantially in the form attached hereto as Schedule 2 duly executed by the Holder, and payment for all applicable transfer taxes (if any). Upon any such registration or transfer, a new warrant to purchase Common Stock in substantially the form of this Warrant (any such new warrant, a "**New Warrant**") evidencing the portion of this Warrant so transferred shall be issued to the transferee, and a New Warrant evidencing the remaining portion of this Warrant not so transferred, if any, shall be issued to the transferring Holder. The acceptance of the New Warrant by the transferee thereof shall be deemed the acceptance by such transferee of all of the rights and obligations in respect of the New Warrant that the Holder has in respect of this Warrant. The Company shall, or will cause its Transfer Agent to, prepare, issue and deliver at the Company's own expense any New Warrant under this Section 3. Until due presentment for registration of transfer, the Company may treat the registered Holder hereof as the owner and holder for all purposes, and the Company shall not be affected by any notice to the contrary.

4. *Exercise of Warrants*.

(a) All or any part of this Warrant shall be exercisable by the registered Holder in any manner permitted by this Warrant (including Section 11) at any time and from time to time on or after the Original Issue Date, and such rights shall not expire.

(b) The Holder may exercise this Warrant by delivering to the Company (i) an exercise notice, in the form attached as Schedule 1 hereto (the "**Exercise Notice**"), completed and duly signed, and (ii) payment of the Exercise Price for the number of Warrant Shares asto which this Warrant is being exercised (which may take the form of a "cashless exercise" if so indicated in the Exercise Notice pursuant to Section 10 below), and the date on which the last of such items is delivered to the Company (as determined in accordance with the notice provisions hereof) is an **"Exercise Date**." The Holder shall not be required to deliver the original Warrant in order to effect an exercise hereunder. Execution and delivery of the Exercise Notice shall have the same effect as cancellation of the original Warrant and issuance of a New Warrant evidencing the right to purchase the remaining number of Warrant Shares, if any.

5. *Delivery of Warrant Shares*.

(a) Upon exercise of this Warrant, the Company shall promptly (but in no event later than the number of Trading Days comprising the Standard Settlement Period following the Exercise Date), upon the request of the Holder, credit such aggregate number of shares of Common Stock specified by the Holder in the Exercise Notice and to which the Holder is entitled pursuant to such exercise (the "**Exercise Shares**") to the Holder's or its designee's balance account with The Depository Trust Company ("**DTC**") through its Deposit Withdrawal At Custodian system, or if the Transfer Agent is then a participant in the DTC Fast Automated Securities Transfer Program (the "**FAST Program**") and either (A) there is an effective registration statement permitting the issuance of the Warrant Shares to or the resale of such Warrant Shares by the Holder or (B) the Exercise Shares are eligible for resale by the Holder without volume or manner-of-sale restrictions pursuant to Rule 144 promulgated under the Securities Act (assuming cashless exercise of this Warrant). If the Transfer Agent is not a member of the FAST Program or if (A) and (B) above are not true, the Transfer Agent will either (i) record the Exercise Shares in the name of the Holder or its designee on the certificates reflecting the Exercise Shares with an appropriate legend regarding restriction on transferability, which shall be issued and dispatched by overnight courier to the address as specified in the Exercise Notice, and on the Company's share register or (ii) issue such Exercise Shares in the name of the Holder or its designee in restricted book-entry form in the Company's share register. The Holder, or any Person so designated by the Holder to receive Warrant Shares, shall be deemed to have become the holder of record of such Warrant Shares as of the Exercise Date, irrespective of the date such Warrant Shares are credited to the Holder's DTC account, the date of the book entry positions or the date of delivery of the certificates evidencing such Exercise Shares, as the case may be.

(b) If the Company fails to deliver to the Holder or its designee Exercise Shares in the manner required pursuant to Section 5(a) within the Standard Settlement Period following the Exercise Date and the Holder purchases (in an open market transaction or otherwise) shares of Common Stock to deliver in satisfaction of a sale by the Holder of the Warrant Shares which the Holder anticipated receiving upon such exercise (a "Buy-In") but did not receive within the Standard Settlement Period, then the Company shall, within two (2) Trading Days after the Holder's request, (A) pay cash to the Holder in an amount equal to the excess (if any) of (x) Holder's total purchase price (including brokerage commissions, if any) for the shares of Common Stock so purchased in the Buy-In, less (y) the product of (1) the number of shares of Common Stock purchased in the Buy-In, times (2) the Closing Sale Price of a share of Common Stock on the Exercise Date, and (B) at the option of the Holder, either reinstate the portion of the Warrant and equivalent number of Warrant Shares for which such exercise was not honored (in which case such exercise shall be deemed rescinded) or deliver to the Holder the number of shares of Common Stock that would have been issued had the Company timely complied with its principal place exercise and delivery obligations hereunder.

(c) To the extent permitted by law and subject to Section5(b), the Company's obligations to issue and deliver Warrant Shares in accordance with and subject to the terms hereof (including the limitations set forth in Section 11 below) are absolute and unconditional, irrespective of any action or inaction by the Holder to enforce the same, any waiver or consent with respect to any provision hereof, the recovery of any judgment against any Person or any action to enforce the same, or any setoff, counterclaim, recoupment, limitation or termination, or any breach or alleged breach by the Holder or any other Person of any obligation to the Company or any violation or alleged violation of law by the Holder or any other Person, and irrespective of any other circumstance that might otherwise limit such obligation of the Company to the Holder in connection with the issuance of Warrant Shares. Subject to Section5(b), nothing herein shall limit the Holder's right to pursue any other remedies available to it hereunder, at law or in equity including, without limitation, a decree of specific performance and/or injunctive relief with respect to the Company's failure to timely deliver shares of Common Stock upon exercise of the Warrant as required pursuant to the terms hereof.

6. *Charges, Taxes and Expenses*. Issuance and delivery of shares of Common Stock upon exercise of this Warrant shall be made without charge to the Holder for any issue or transfer tax, transfer agent fee or other incidental tax or expense (excluding any applicable stamp duties) in respect of the issuance of such shares, all of which taxes and expenses shall be paid by the Company; *provided*, *however*, that the Company shall not be required to pay any tax that may be payable in respect of any transfer involved in the registration of

any Warrant Shares or the Warrants in a name other than that of the Holder or an Affiliate thereof. The Holder shall be responsible for all other tax liability that may arise as a result of holding or transferring this Warrant or receiving Warrant Shares upon exercise hereof.

7. *Replacement of Warrant*. If this Warrant is mutilated, lost, stolen or destroyed, the Company shall issue or cause to be issued in exchange and substitution for and upon cancellation hereof, or in lieu of and substitution for this Warrant, a New Warrant, but only upon receipt of evidence reasonably satisfactory to the Company of such loss, theft or destruction (in such case) and, in each case, a customary and reasonable contractual indemnity, if requested by the Company. If a New Warrant is requested as a result of a mutilation of this Warrant, then the Holder shall deliver such mutilated Warrant to the Company as a condition precedent to the Company's obligation to issue the New Warrant.

8. *Reservation of Warrant Shares*. The Company covenants that it will, at all times while this Warrant is outstanding, reserve and keep available out of the aggregate of its authorized but unissued and otherwise unreserved Common Stock, solely for the purpose of enabling it to issue Warrant Shares upon exercise of this Warrant as herein provided, the number of Warrant Shares that are initially issuable and deliverable upon the exercise of this entire Warrant, free from preemptive rights or any other contingent purchase rights of persons other than the Holder (taking into account the adjustments and restrictions of Section 9). The Company covenants that all Warrant Shares so issuable and deliverable shall, upon issuance and the payment of the applicable Exercise Price in accordance with the terms hereof, be duly and validly authorized, issued and fully paid and non-assessable. The Company will take all such action as may be reasonably necessary to assure that such shares of Common Stock may be issued as provided herein without violation of any applicable law or regulation, or of any requirements of any securities exchange or automated quotation system upon which the Common Stock may be listed. The Company further covenants that it will not, without the prior written consent of the Holder, take any actions to increase the par value of the Common Stock at any time while this Warrant is outstanding.

9. *Certain Adjustments*. The Exercise Price and number of Warrant Shares issuable upon exercise of this Warrant (the "Number of Warrant Shares") are subject to adjustment from time to time as set forth in this Section 9.

(a) Stock Dividends and Splits. If the Company, at any time while this Warrant is outstanding, (i) pays a stock dividend on its Common Stock or otherwise makes a distribution on any class of capital stock issued and outstanding on the Original Issue Date and in accordance with the terms of such stock on the Original Issue Date or as amended, that is payable in shares of Common Stock, (ii) subdivides its outstanding shares of Common Stock into a larger number of shares of Common Stock, (iii) combines its outstanding shares of Common Stock into a smaller number of shares of Common Stock or (iv) issues by reclassification of shares of capital stock any additional shares of Common Stock of the Company, then in each such case the Number of Warrant Shares shall be multiplied by a fraction, the numerator of which shall be the number of shares of Common Stock outstanding immediately after such event and the denominator of which shall be the number of shares of Common Stock outstanding immediately before such event. Any adjustment made pursuant to clause (i) of this paragraph shall become effective immediately after the record date for the determination of stockholders entitled to receive such dividend or distribution, provided, however, that if such record date shall have been fixed and such dividend is not fully paid on the date fixed therefor, the Exercise Price shall be recomputed accordingly as of the close of business located on such record date and thereafter the Exercise Price shall be adjusted pursuant to this paragraph as of the time of actual payment of such dividends. Any adjustment pursuant to clause (ii), (iii) or (iv) of this paragraph shall become effective immediately after the effective date of such subdivision, combination or issuance.

(b) Pro Rata Distributions. If, on or after the Original Issue Date, the Company shall declare or make any dividend or other pro rata distribution of its assets (or rights to acquire its assets) to holders of shares of Common Stock, by way of return of capital or otherwise (including, without limitation, any distribution of cash, stock or other securities, property, options, evidence of indebtedness or any other assets by way of a dividend, spin off, reclassification, corporate rearrangement, scheme of arrangement or other similar transaction, but, for the avoidance of doubt, excluding any distribution of shares of Common Stock subject to Section 9(a), any distribution of Purchase Rights (as defined below) subject to Section 9(c) and any Fundamental Transaction (as defined below) subject to Section 9(d)) (a "**Distribution**") then, in each such case, the Holder shall be entitled to participate in such Distribution to the same extent that the Holder would have participated therein if the Holder had held the number of shares of Common Stock acquirable upon complete exercise of this Warrant (without regard to any limitations or restrictions on exercise of this Warrant, including without limitation, the Maximum Percentage (as defined below)) immediately before the date on which a record is taken for such Distribution, or, if no such record is taken, the date as of which the record holders of shares of Common Stock are to be determined for the participation in such Distribution (provided, that to the extent that the Holder's right to participate in any such Distribution would result in the Holder and the other Attribution Parties exceeding the Maximum Percentage, then the Holder shall not be entitled to participate in such Distribution to such extent (and shall not be entitled to beneficial ownership of such shares of Common Stock as a result of such Distribution (and beneficial ownership) to such extent) and the portion of such Distribution shall be held in abeyance for the benefit of the Holder until such time or times as its right thereto would not result in the Holder and the other Attribution Parties exceeding the Maximum Percentage, at which time or times the Holder shall be granted such Distribution (and any Distributions declared or made on such initial Distribution or on any subsequent Distribution held similarly in abeyance) to the same extent as if there had been no such limitation).

(c) Purchase Rights. If at any time on or after the Original Issue Date, the Company grants, issues or sells any Options, Convertible Securities or rights to purchase stock, warrants, securities or other property, in each case pro rata to the record holders of any class of Common Stock (the "**Purchase Rights**"), then the Holder will be entitled to acquire, upon the terms applicable to such Purchase Rights, the aggregate Purchase Rights which the Holder could have acquired if the Holder had held the number of shares of Common Stock acquirable upon complete exercise of this Warrant (without regard to any limitations or restrictions on exercise of this Warrant, including without limitation, the Maximum Percentage) immediately before the date on which a record is taken for the grant, issuance or sale of such Purchase Rights, or, if no such record is taken, the date as of which the record holders of Common Stock are to be determined for the grant, issuance or sale of such Purchase Rights (provided, that to the extent that the Holder's right to participate in any such Purchase Right would result in the Holder and the other Attribution Parties exceeding the Maximum Percentage, then the Holder shall not be entitled to

participate in such Purchase Right to such extent (and shall not be entitled to beneficial ownership of such Common Stock as a result of such Purchase Right (and beneficial ownership) to such extent) and such Purchase Right to such extent shall be held in abeyance for the benefit of the Holder until such time or times as its right thereto would not result in the Holder and the other Attribution Parties exceeding the Maximum Percentage, at which time or times the Holder shall be granted such right (and any Purchase Right granted, issued or sold on such initial Purchase Right or on any subsequent Purchase Right to be held similarly in abeyance) to the same extent as if there had been no such limitation). As used in this Section 9(c), (i) "Options" means any rights, warrants or options to subscribe for or purchase shares of Common Stock or Convertible Securities and (ii) "Convertible Securities" mean any stock or securities (other than Options) directly or indirectly convertible into or exercisable or exchangeable for shares of Common Stock.

(d) Fundamental Transactions. If, at any time while this Warrant is outstanding (i) the Company effects any merger or consolidation of the Company with or into another Person, in which the Company is not the surviving entity or in which the stockholders of the Company immediately prior to such merger or consolidation do not own, directly or indirectly, at least 50% of the voting power of the surviving entity immediately after such merger or consolidation, (ii) the Company effects any sale to another Person of all or substantially all of its assets in one transaction or a series of related transactions, (iii) pursuant to any tender offer or exchange offer (whether by the Company or another Person), holders of capital stock tender shares representing more than 50% of the voting power of the capital stock of the Company and the Company or such other Person, as applicable, accepts such tender for payment, (iv) the Company consummates a stock purchase agreement or other business combination (including, without limitation, a reorganization, recapitalization, spin-off or scheme of arrangement) with another Person whereby such other Person acquires more than 50% of the voting power of the capital stock of the Company (except for any such transaction in which the stockholders of the Company immediately prior to such transaction maintain, in substantially the same proportions, the voting power of such Person immediately after the transaction) or (v) the Company effects any reclassification of the Common Stock or any compulsory share exchange pursuant to which the Common Stock is effectively converted into or exchanged for other securities, cash or property (other than as a result of a subdivision or combination of shares of Common Stock covered by Section 9(a) above) (in any such case, a "**Fundamental Transaction**"), then following such Fundamental Transaction the Holder shall have the right to receive, upon exercise of this Warrant, the same amount and kind of securities, cash or property as it would have been entitled to receive upon the occurrence of such Fundamental Transaction if it had been, immediately prior to such Fundamental Transaction, the holder of the number of Warrant Shares then issuable upon exercise in full of this Warrant without regard to any limitations on exercise contained herein (the "**Alternate Consideration**"). The Company shall not effect any Fundamental Transaction in which the Company is not the surviving entity or the Alternate Consideration includes securities of another Person unless (i) the Alternate Consideration is solely cash and the Company provides for the simultaneous "cashless exercise" of this Warrant pursuant to Section 10 below or (ii) prior to or simultaneously with the consummation thereof, any successor to the Company, surviving entity or other Person (including any purchaser of assets of the Company) shall assume the obligation to deliver to the Holder such Alternate Consideration as, in accordance with the foregoing provisions, the Holder may be entitled to receive, and the other obligations under this Warrant. The provisions of this paragraph (c) shall similarly apply to subsequent transactions analogous of a Fundamental Transaction type.

(e) Number of Warrant Shares. Simultaneously with any adjustment to the Exercise Price pursuant to Section 9, the number of Warrant Shares that may be purchased upon exercise of this Warrant shall be increased or decreased proportionately, so that after such adjustment the aggregate Exercise Price payable hereunder for the increased or decreased number of Warrant Shares shall be the same as the aggregate Exercise Price in effect immediately prior to such adjustment.

(f) Calculations. All calculations under this Section 9 shall be made to the nearest one-tenth of one cent or the nearest share, as applicable.

(g) Notice of Adjustments. Upon the occurrence of each adjustment pursuant to this Section 9, the Company at its expense will, at the written request of the Holder, promptly compute such adjustment, in good faith, in accordance with the terms of this Warrant and prepare a certificate setting forth such adjustment, including a statement of the adjusted Exercise Price and adjusted number or type of Warrant Shares or other securities issuable upon exercise of this Warrant (as applicable), describing the transactions giving rise to such adjustments and showing in detail the facts upon which such adjustment is based. Upon written request, the Company will promptly deliver a copy of each such certificate to the Holder and to the Company's transfer agent.

(h) Notice of Corporate Events. If, while this Warrant is outstanding, the Company (i) declares a dividend or any other distribution of cash, securities or other property in respect of its Common Stock, including, without limitation, any granting of rights or warrants to subscribe for or purchase any capital stock of the Company or any subsidiary, (ii) authorizes or approves, enters into any agreement contemplating or solicits stockholder approval for any Fundamental Transaction or (iii) authorizes the voluntary dissolution, liquidation or winding up of the affairs of the Company, then the Company shall deliver to the Holder a notice of such transaction at least ten (10) days prior to the applicable record or effective date on which a Person would need to hold Common Stock in order to participate in or vote with respect to such transaction; provided, however, that the failure to deliver such notice or any defect therein shall not affect the validity of the corporate action required to be described in such notice. In addition, if while this Warrant is outstanding, the Company authorizes or approves, enters into any agreement contemplating or solicits stockholder approval for any Fundamental Transaction contemplated by Section 9(d), other than a Fundamental Transaction under clause (iii) of Section 9(d), the Company shall deliver to the Holder a notice of such Fundamental Transaction at least thirty (30) days prior to the date such Fundamental Transaction is consummated. Holder agrees to maintain any information disclosed pursuant to this Section 9(h) in confidence until such information is publicly available, and shall comply with applicable law with respect to trading in the Company's securities following receipt of any such information.

10. *Payment of Exercise Price*. Notwithstanding anything contained herein to the contrary, the Holder may, in its sole discretion, satisfy its obligation to pay the Exercise Price through a "cashless exercise", in which event the Company shall issue to the Holder the number of Warrant Shares in an exchange of securities effected pursuant to Section 3(a)(9) of the Securities Act, as determined as follows:

X = Y [(A-B)/A]

where:

"X" equals the number of Warrant Shares to be issued to the Holder;

"Y" equals the total number of Warrant Shares with respect to which this Warrant is then being exercised;

"A" equals the Closing Sale Price of the shares of Common Stock (as reported by Bloomberg Financial Markets) as of the Trading Day on the date immediately preceding the Exercise Date; and

"B" equals the Exercise Price then in effect for the applicable Warrant Shares at the time of such exercise.

For purposes of Rule 144 promulgated under the Securities Act, it is intended, understood and acknowledged that the Warrant Shares issued in a "cashless exercise" transaction shall be deemed to have been acquired by the Holder, and the holding period for the Warrant Shares shall be deemed to have commenced, on the date this Warrant was originally issued (provided that the Commission continues to take the position that such treatment is proper at the time of such exercise). In the event that a registration statement registering the issuance of Warrant Shares is, for any reason, not effective at the time of exercise of this Warrant, then the Warrant may only be exercised through a cashless exercise, as set forth in this Section10. If the Warrant Shares are issued in such a cashless exercise, the Company acknowledges and agrees that, in accordance with Section 3(a)(9) of the Securities Act, the Exercise Shares issued in such exercise may be tacked on to the holding period of the Warrants being exercised. Except as set forth in Section 5(b) (Buy-In remedy) and Section 12 (payment of cash in lieu of fractional shares), in no event will the exercise of this Warrant be settled in cash.

11. *Limitations on Exercise*.

(a) Notwithstanding anything to the contrary contained herein, the Company shall not effect the exercise of any portion of this Warrant, and the Holder of the Warrant shall not have the right to exercise any portion of the Warrant, and any such exercise shall be null and void ab initio and treated as if the exercise had not been made, to the extent that immediately prior to or following such exercise, the Holder, together with the Attribution Parties, beneficially owns or would beneficially own as determined in accordance with Section 13(d) of the Exchange Act and the rules promulgated thereunder, in excess of 4.99% (the "**Maximum Percentage**") of the Common Stock that would be issued and outstanding following such exercise. For purposes of calculating beneficial ownership for determining whether the Maximum Percentage is or will be exceeded, the aggregate number of shares of Common Stock held and/or beneficially owned by the Holder together with the Attribution Parties, shall include the number of shares of Common Stock held and/or beneficially owned by the Holder together with the Attribution Parties plus the number of shares of Common Stock issuable upon exercise of the relevant Warrant with respect to which the determination is being made but shall exclude the number of shares of Common Stock which would be issuable upon (i) exercise of the remaining, unexercised Warrant held and/or beneficially owned by the Holder or the Attribution Parties and (ii) exercise or conversion of the unexercised or unconverted portion of any other securities of the Company held and/or beneficially owned by such Holder or any Attribution Party (including, without limitation, any convertible notes, convertible stock or warrants) that are subject to a limitation on conversion or exercise analogous to the limitation contained herein. For purposes of this Paragraph 11(a), beneficial ownership of the Holder or the Attribution Parties shall, except as set forth in the immediately preceding sentence, be calculated and determined in accordance with Section 13(d) of the Exchange Act and the rules promulgated thereunder. For purposes of the Warrant, in determining the number of outstanding shares of Common Stock, a Holder of the Warrant may rely on the number of outstanding shares of Common Stock as reflected in (1) the Company's most recent Form 10-K, Form 10-Q, Current Report on Form 8-K or other public filing with the Securities and Exchange Commission, as the case may be, (2) a more recent public announcement by the Company or (3) any other notice by the Company or the Company's transfer agent setting forth the number of shares of Common Stock outstanding (such issued and outstanding shares, the "**Reported Outstanding Share Number**"). For any reason at any time, upon the written or oral request of the Holder, the Company shall within one (1) Business Day confirm orally and in writing or by electronic mail to the Holder the number of shares of Common Stock then outstanding. The Holder shall disclose to the Company the number of shares of Common Stock that it, together with the Attribution Parties, holds and/or beneficially owns and has the right to acquire through the exercise of derivative securities and any limitations on exercise or conversion analogous to the limitation contained herein contemporaneously or immediately prior to submitting an Exercise Notice for the relevant Warrant. If the Company receives an Exercise Notice from the Holder at a time when the actual number of outstanding shares of Common Stock is less than the Reported Outstanding Share Number, the Company shall (i) notify the Holder in writing of the number of shares of Common Stock then outstanding and, to the extent that such Exercise Notice would otherwise cause the Holder's, together with the Attribution Parties', beneficial ownership, as determined pursuant to this Section 11(a), to exceed the Maximum Percentage, the Holder must notify the Company of a reduced number of Warrant Shares to be purchased pursuant to such Exercise Notice (the number of shares by which such purchase is reduced, the "Reduction Shares") and (ii) as soon as reasonably practicable, the Company shall return to the Holder any exercise price paid by the Holder for the Reduction Shares. In any case, the number of outstanding shares of Common Stock shall be determined after giving effect to the conversion or exercise of securities of the Company, including this Warrant, by the Holder and the Attribution Parties since the date as of which the Reported Outstanding Share Number was reported. In the event that the issuance of Common Stock to the Holder upon exercise of this Warrant results in the Holder, together with the Attribution Parties, being deemed to beneficially own, in the aggregate, more than the Maximum Percentage of the number of outstanding shares of Common Stock (as determined under Section 13(d) of the Exchange Act), the number of shares so issued by which the Holder's, together with the Attribution Parties', aggregate beneficial ownership exceeds the Maximum Percentage (the "Excess Shares") shall be deemed null and void and shall be cancelled ab initio, and the Holder and/or the Attribution Parties shall not have the power to vote or to transfer the Excess Shares. As soon as reasonably practicable after the issuance of the Excess Shares has been deemed null and void, the Company shall return to the Holder the exercise price paid by the Holder for the Excess Shares. By written notice to the Company, a Holder of the Warrant may from time to time increase or decrease the Maximum Percentage to any other percentage not in excess of 19.99% specified in such notice; provided that any increase in the Maximum Percentage will not be effective until the sixty-first (61st) day after such notice is delivered to the Company and shall not negatively affect any partial exercise effected prior to such change.

(b) This Section 11 shall not restrict the number of shares of Common Stock which a Holder or the Attribution Parties may receive or beneficially own in order to determine the amount of securities or other consideration that such Holder or the Attribution Parties may receive in the event of a Fundamental Transaction as contemplated in Section 9(c) of this Warrant. For purposes of clarity, the shares of Common Stock issuable pursuant to the terms of this Warrant in excess of the Maximum Percentage shall not be deemed to be beneficially owned by the Holder or the Attribution Parties for any purpose including for purposes of Section 13(d) of the Exchange Act and the rules promulgated thereunder, including Rule 16a-1(a)(1). No prior inability to exercise this Warrant pursuant to this Section 11 shall have any effect on the applicability of the provisions of this Section 11 with respect to any subsequent determination of exercisability. The provisions of this Section 11shall be construed and implemented in a manner otherwise than in strict conformity with the terms of this Section 11 to the extent necessary to correct this Section 11 or any portion of this Section 11which may be defective or inconsistent with the intended beneficial ownership limitation contained in this Section 11 or to make changes or supplements necessary or desirable to properly give effect to such limitation. The limitation contained in this Section 11 may not be waived and shall apply to a successor holder of this Warrant.

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12. *No Fractional Shares*. No fractional Warrant Shares will be issued in connection with any exercise of this Warrant. In lieu of any fractional shares that would otherwise be issuable, the number of Warrant Shares to be issued shall be rounded down to the next whole number and the Company shall pay the Holder in cash the fair market value (based on the Closing Sale Price) for any such fractional shares.

13. *Notices*. Any and all notices or other communications or deliveries hereunder (including, without limitation, any Exercise Notice) shall be in writing and shall be deemed given and effective on the earliest of (i) the date of transmission, if such notice or communication is delivered confirmed e-mail at the e-mail address specified in the books and records of the Transfer Agent prior to 5:30 P.M., New York City time, on a Trading Day, (ii) the next Trading Day after the date of transmission, if such notice or communication is delivered via confirmed e-mail at the e-mail address specified in the books and records of the Transfer Agent on a day that is not a Trading Day or later than 5:30 P.M., New York City time, on any Trading Day, (iii) the Trading Day following the date of mailing, if sent by nationally recognized overnight courier service specifying next business day delivery, or (iv) upon actual receipt by the Person to whom such notice is required to be given, if by hand delivery. Notice to the Company shall be delivered, mailed or sent to Denali Therapeutics Inc., 161 Oyster Point Blvd., South San Francisco, California 94080, (" Attention: President and Chief Executive Officer.

14. *Denali Warrant Agent*"), Biogen MA, Inc., . The Company shall initially serve as warrant agent under this Warrant. Upon thirty (30) days' notice to the Holder, the Company may appoint a new warrant agent. Any corporation organized into which the Company or any new warrant agent may be merged or any corporation resulting from any consolidation to which the Company or any new warrant agent shall be a party or any corporation to which the Company or any new warrant agent transfers substantially all of its corporate trust or shareholders services business shall be a successor warrant agent under this Warrant without any further act. Any such successor warrant agent shall promptly cause notice of its succession as warrant agent to be mailed (by first class mail, postage prepaid) to the laws of Holder at the Commonwealth of Massachusetts having an office at 225 Binney Street, Cambridge, MA 02142 (" Holder's last address as shown on the Warrant Register.

15. *BIMA Miscellaneous*"), and Biogen International GmbH, a Gesellschaft mit beschränkter Haftung organized under the laws of Switzerland, whose registered office is at Neuhofstrasse 30, 6340 Baar, Switzerland ("BIG", together with BIMA, collectively, "Biogen").

Reference is also hereby made to the Right of First Negotiation, Option, and License Agreement, dated October 6, 2020 (the " (a) ROFN, Option, and License Agreement"), by and among Denali and Biogen.

This Amendment to the LRRK2 Agreement and Waiver of and Amendment to the ROFN, Option, and License Agreement (the "Amendment"), dated August 17, 2023 (the "Amendment Effective Date"), amends the LRRK2 Agreement and waives certain rights and amends certain provisions under the ROFN, Option and License Agreement.

Biogen and Denali are each separately referred to No Rights as a " StockholderParty" and are collectively referred to . Except as the "Parties". Capitalized terms not defined herein shall have the meaning otherwise set forth in this Warrant, the LRRK2 Agreement Holder, solely in such Person's capacity as a holder of this Warrant, shall not be entitled to vote or receive dividends or be deemed the ROFN, Option, and License Agreement, holder of share capital of the Company for any purpose, nor shall anything contained in this Warrant be construed to confer upon the Holder, solely in such Person's capacity as applicable. the Holder of this Warrant, any of the rights of a stockholder of the Company or any right to vote, give or withhold consent to any corporate action (whether any reorganization, issue of stock, reclassification of stock, consolidation, merger, amalgamation, conveyance or otherwise), receive notice of meetings, receive dividends or subscription rights, or otherwise, prior to the issuance to the Holder of the Warrant Shares which such Person is then entitled to receive upon the due exercise of this Warrant. In addition, nothing contained in this Warrant shall be construed as imposing any liabilities on the Holder to purchase any securities (upon exercise of this Warrant or otherwise) or as a stockholder of the Company, whether such liabilities are asserted by the Company or by creditors of the Company.

The Parties agree as follows:

Section 1. (b) Amendments to LRRK2 Agreement Authorized Shares.

Section 1.1 Close-Out (i) Except and to the extent as waived or consented to by the Holder, the Company shall not by any action, including, without limitation, amending its certificate or articles of LIGHTHOUSE Study and Review incorporation or through any reorganization, transfer of LUMA Study; Independent Studies. The

updated Global Development Plan/Budget assets, consolidation, merger, dissolution, issue or sale of securities or any other voluntary action, avoid or seek to avoid the observance or performance of any of the LRRK2 Agreement is set forth on *Exhibit A* terms of this Warrant, but will at all times in good faith assist in the carrying out of all such terms and in the taking of all such actions as may be necessary or appropriate to this Amendment and has been reviewed and approved by protect the JSC rights of Holder as set forth in Section 3.1.2 (Amendments and Updates) this Warrant against impairment. Without limiting the generality of the LRRK2 Agreement. Denali foregoing, the Company will (a) not increase the par value of any Warrant Shares above the amount payable therefor upon such exercise immediately prior to such increase in par value, (b) take all such action as may but be necessary or appropriate in order that the Company may validly and legally issue fully paid and non-assessable Warrant Shares upon the exercise of this Warrant, and (c) use commercially reasonable efforts to obtain all such authorizations, exemptions or consents from any public regulatory body having jurisdiction thereof as may be necessary to enable the Company to perform its obligations under this Warrant.

(ii) Before taking any action which would result in an adjustment in the number of Warrant Shares for which this Warrant is exercisable or in the Exercise Price, the Company shall obtain all such authorizations or exemptions thereof, or consents thereto, as may be necessary from any public regulatory body or bodies having jurisdiction thereof.

(c) Successors and Assigns. Subject to compliance with applicable securities laws and restrictions on transfer set forth in this Warrant, this Warrant may be assigned by the Holder. This Warrant may not obligated to, conduct an Independent Study of Licensed Product solely in LRRK2-PD Patients. [***]

Section 1.2 Revisions to Section 3.1.3 (Development Effort).

The phrase [***] in each case ((i) and (ii)),” in Sections 3.1.3(a)(ii) and 3.1.3(a)(iii) be assigned by the Company without the written consent of the LRRK2 Agreement Holder, except to a successor in the event of a Fundamental Transaction. This Warrant shall be binding on and inure to the benefit of the Company and the Holder and their respective successors and assigns. Subject to the preceding sentence, nothing in this Warrant shall be construed to give to any Person other than the Company and the Holder any legal or equitable right, remedy or cause of action under this Warrant. This Warrant may be amended only in writing signed by the Company and the Holder, or their successors and assigns.

(d) Amendment and Waiver. Except as otherwise provided herein, the provisions of the Warrants may be amended and the Company may take any action herein prohibited, or omit to perform any act herein required to be performed by it, only if the Company has obtained the written consent of the Holder.

(e) Acceptance. Receipt of this Warrant by the Holder shall constitute acceptance of and agreement to all of the terms and conditions contained herein.

(f) Governing Law; Jurisdiction. ALL QUESTIONS CONCERNING THE CONSTRUCTION, VALIDITY, ENFORCEMENT AND INTERPRETATION OF THIS WARRANT SHALL BE GOVERNED BY AND CONSTRUED AND ENFORCED IN ACCORDANCE WITH THE LAWS OF THE STATE OF NEW YORK WITHOUT REGARD TO THE PRINCIPLES OF CONFLICTS OF LAW THEREOF. EACH OF THE COMPANY AND THE HOLDER HEREBY IRREVOCABLY SUBMITS TO THE EXCLUSIVE JURISDICTION OF THE STATE AND FEDERAL COURTS SITTING IN THE CITY OF NEW YORK, BOROUGH OF MANHATTAN, FOR THE ADJUDICATION OF ANY DISPUTE HEREUNDER OR IN CONNECTION HEREWITH OR WITH ANY TRANSACTION CONTEMPLATED HEREBY OR DISCUSSED HEREIN (INCLUDING WITH RESPECT TO THE ENFORCEMENT OF ANY OF THE TRANSACTION DOCUMENTS), AND HEREBY IRREVOCABLY WAIVES, AND AGREES NOT TO ASSERT IN ANY SUIT, ACTION OR PROCEEDING, ANY CLAIM THAT IT IS NOT PERSONALLY SUBJECT TO THE JURISDICTION OF ANY SUCH COURT. EACH OF THE COMPANY AND THE HOLDER HEREBY IRREVOCABLY WAIVES PERSONAL SERVICE OF PROCESS AND CONSENTS TO PROCESS BEING SERVED IN ANY SUCH SUIT, ACTION OR PROCEEDING BY MAILING A COPY THEREOF VIA REGISTERED OR CERTIFIED MAIL OR OVERNIGHT DELIVERY (WITH EVIDENCE OF DELIVERY) TO SUCH PERSON AT THE ADDRESS IN EFFECT FOR NOTICES TO IT AND AGREES THAT SUCH SERVICE SHALL CONSTITUTE GOOD AND SUFFICIENT SERVICE OF PROCESS AND NOTICE THEREOF. NOTHING CONTAINED HEREIN SHALL BE DEEMED TO LIMIT IN ANY WAY ANY RIGHT TO SERVE PROCESS IN ANY MANNER PERMITTED BY LAW. EACH OF THE COMPANY AND THE HOLDER HEREBY WAIVES ALL RIGHTS TO A TRIAL BY JURY.

(g) Headings. The headings herein are for convenience only, do not constitute a part of this Warrant and shall not be deemed to limit or affect any of the provisions hereof.

(h) Severability. In case any one or more of the provisions of this Warrant shall be invalid or unenforceable in any respect, the validity and enforceability of the remaining terms and provisions of this Warrant shall not in any way be affected or impaired thereby, and the Company and the Holder will attempt in good faith to agree upon a valid and enforceable provision which shall be a commercially reasonable substitute therefor, and upon so agreeing, shall incorporate such substitute provision in this Warrant. It is hereby deleted, stipulated and in those places, declared to be the phrase [***], in each case ((i) intention of the parties that they would have executed the remaining terms, provisions, covenants and (ii)),” is hereby inserted, restrictions without including any of such that those sections shall read as follows:

“**(ii)Co-Commercialization Territory**. Each Party (and in the case of Denali, to the extent permitted under this Definitive LRRK2 Agreement) will use Commercially Reasonable Efforts to seek and obtain Regulatory Approval for at least [***], in each case ((i) and (ii)), [***]. may be hereafter declared invalid, illegal, void or unenforceable.

(iii) Ex-Co-Commercialization Territory. Biogen will use Commercially Reasonable Efforts to seek and obtain Regulatory Approval for at least [***], in each case ((i) and (ii), [***].

Section 1.3 Revisions to Section 3.1.4(e)(iii). Section 3.1.4(e)(iii) (Regulatory Approval) is hereby amended to add the following at the end of that section:

“Notwithstanding the foregoing, if Biogen is the Declining Party and Denali conducts any Independent Study directed to a Licensed Product in [***], then: [REMAINDER OF PAGE INTENTIONALLY LEFT BLANK]

[***] Certain information in this document has been omitted from this exhibit because it is both (i) not material and (ii) would be competitively harmful if publicly disclosed.

---

(1) If Denali receives Regulatory Approval for a Licensed Product in [***] in any country utilizing any data generated from such Independent Study and Biogen (i) is conducting, actively preparing to conduct, or analyzing the results of [***] a Clinical Study, (ii) is actively preparing to submit [***], or has submitted, all Regulatory Documentation for a Licensed Product to a Regulatory Authority [***] reasonably necessary for obtaining Regulatory Approval (subject to any such further requests as may be provided by such Regulatory Authority with respect to such Licensed Product), or (iii) has obtained Regulatory Approval, in each case (i)-(iii), [***] shall be payable by Biogen to Denali unless and until Biogen provides an Independent Study Opt-In Notice as contemplated by Section 3.1.4(e) (Opt-In for Independent Study) (and in no event will any such payment be triggered by a Regulatory Approval Update unless an Independent Study Opt-In Notice has been provided by Biogen to the JDC); *provided*, that [***], unless Biogen has provided an Independent Study Opt-In Notice to the JDC as contemplated by Section 3.1.4(e) (Opt-In for Independent Study); and (b) Denali will have the right [***], but in no event will a Regulatory Approval Update be deemed to occur unless Biogen has provided an Independent Study Opt-In Notice to the JDC as contemplated by Section 3.1.4(e) (Opt-In for Independent Study).

(2) If Denali receives Regulatory Approval for a Licensed Product in [***] in any country utilizing any data generated from such Independent Study and Biogen (i) is not conducting, not actively preparing IN WITNESS WHEREOF, the Company has caused this Warrant to conduct, or not actively analyzing the results of [***] a Clinical Study, (ii) is not actively preparing to submit [***], or has not submitted, all Regulatory Documentation for a Licensed Product to a Regulatory Authority [***] reasonably necessary for obtaining Regulatory Approval (subject to any such further requests be duly executed by its authorized officer as may be provided by such Regulatory Authority with respect to such Licensed Product), and (iii) has not obtained Regulatory Approval, in each case (i)-(iii) [***] then Biogen will promptly submit an Independent Study Opt-In Notice to the JDC as contemplated by Section 3.1.4(e) (Opt-In for Independent Study)."

Section 1.4 Revisions to PD Development Milestone Payments (Section 7.2.1). The table set forth in Section 7.2.1 (PD Development Milestone Payments) of the LRRK2 Agreement is hereby deleted, and in its place, the following table is inserted:date first indicated above.

PD Development Milestone Event	***PD Development Milestone Payment (US$)***
1. *[Intentionally omitted]*	*[Intentionally omitted]*
1. *[Intentionally omitted]*	*[Intentionally omitted]*
1. *[Intentionally omitted]*	*[Intentionally omitted]*
4. [***]	[***]
5. [***]	[***]

The definition of [***] in Section 7.2.1 (PD Development Milestone Payments) of the LRRK2 Agreement is hereby deleted, and in its place, the following is inserted: [***].

The definition of [***] in Section 7.2.1 (PD Development Milestone Payments) of the LRRK2 Agreement is hereby deleted, and in its place, the following is inserted: [***].

The definitions of [***] in Section 7.2.1 (PD Development Milestone Payments) of the LRRK2 Agreement are hereby deleted, and in their place, the following is inserted: "*[Intentionally omitted]*".

[***] Certain information in this document has been omitted from this exhibit because it is both (i) not material and (ii) would be competitively harmful if publicly disclosed.

Section 1.5 Revisions to Section 0 (PD Milestone Details) (Section 7.2.2) and Section 0 (PD Commercial Milestone Payments) (Sections 7.2.3 and 7.10.4). The phrase "Section 0 (PD Milestone Details)" in Section 7.2.2 of the LRRK2 Agreement is hereby deleted, and in its place, the phrase "Section 7.2.3 (PD Milestone Details)" is hereby inserted, and the phrase "Section 0 (PD Commercial Milestone Payments) in Sections 7.2.3 and 7.10.4 of the LRRK2 Agreement is hereby deleted, and in its place, the phrase "Section 7.2.2 (PD Commercial Milestone Payments)" is hereby inserted. The following sentence is hereby added immediately after the definition of [***] in Section 7.2." "If the following milestones in the PD Commercial Milestone table set forth above [***] as amended."

Section 1.6 Revisions to PD Milestone Details (Section 7.2.3).

Section 7.2.3(a) of the LRRK2 Agreement is hereby deleted, and in its place, the following is inserted:

"The Licensed Product with respect to which either of PD Development Milestones Events [***] is achieved or any of [***] is achieved, in each case, may, but need not, be the same Licensed Product."

The third sentence of Section 7.2.3(b) of the LRRK2 Agreement is hereby amended to delete [***]. The fourth sentence of Section 7.2.3(b) of the LRRK2 Agreement is hereby amended to [***]. As a result, those two sentences shall read as follows: [***]

Section 7.2.3(c) of the LRRK2 Agreement is hereby deleted, and in its place, the following is hereby inserted "Except as set forth in Section 7.2.3(f), PD Development Milestone Payment [***] is achieved before the achievement of PD Development Milestone [***]; *provided* that if PD Development Milestone Payment [***] conducted by Denali, then notwithstanding the provisions of Section 3.1.4(d)(i) (Performance of Independent Study) and Section 3.1.4(e)(iii) (Regulatory Approval), PD Development Milestone Payment [***] as contemplated by Section 3.1.4(e) (Opt-In for Independent Study), as amended, and will not be triggered by a Regulatory Approval Update unless Biogen [***].

The words "and Biogen [***] shall be added to Section 7.2.3(e) of the LRRK2 Agreement at the end of clause (i), such that Section 7.2.3(e) shall read as follows:

"The PD Commercial Milestone Events shall be deemed to be achieved for [***].

Section 1.7 Waiver of Section 7.2.3(h).

Section 7.2.3(h) of the LRRK2 Agreement is hereby deleted, and in its place the following is hereby inserted "*[Intentionally omitted.]*"

Section 1.8 Revisions to PD Milestones Payable Once; Maximum Amount (Section 7.2.4).

Section 7.2.4(c) of the LRRK2 Agreement is hereby deleted, and in its place, the following is inserted:

"In no event shall PD Development Milestone Payments paid under Section 7.2.1 (PD Development Milestone [***] in the aggregate (the "**Maximum Development Milestone Amount**") and in no event shall PD Commercial Milestone Payments paid under Section 7.2.2 (PD Commercial Milestone Payments) with respect to Licensed Products exceed [***] in the aggregate (the "**Maximum Commercial Milestone Amount**")."

Section 1.9 Revisions to Non-PD Milestones (Section 7.3.1).

The table set forth in Section 7.3.1 of the LRRK2 Agreement is hereby deleted in its entirety, and in its place, the following is inserted:

[***] Certain information in this document has been omitted from this exhibit because it is both (i) not material and (ii) would be competitively harmful if publicly disclosed.

PD Development Milestone Event	Milestone Payment for Major Indications ($US)	Milestone Payment for Minor Indications (US$)
[***]		
		[***]
	[***]	[***]

[***] DENALI THERAPEUTICS INC.

[***] By: [***] [***]

Name:

Title:

Section 1.10 Revisions to Non-PD Milestones Payable Once; Maximum Amount (Section 7.3.4).

The dollar amount [***] in the third sentence of Section 7.3.4 of the LRRK2 Agreement is hereby deleted, and in its place, dollar amount [***] is hereby inserted, such that the third sentence of Section 7.3.4 of the LRRK2 Agreement shall read as follows:

"In no event shall Non-PD Development Milestone Payments paid under Section 7.3.1 (Non-PD Development Milestone Payments) with respect to Licensed Products exceed [***] in the aggregate and in no event shall Non-PD Commercial Milestone Payments paid under Section 7.3.2 (Non-PD Commercial Milestone Payments) with respect to Licensed Products exceed [***].

Section 1.11 Ratification and Confirmation of LRRK2 Agreement.

The LRRK2 Agreement, except where explicitly amended by this Amendment, will remain unchanged and in full force and effect and is in all respects agreed to, ratified, and confirmed hereby. Any reference to the LRRK2 Agreement after the Amendment Effective Date will be deemed to be a reference to the LRRK2 Agreement, as amended by this Amendment.

Section 2. Waiver of Certain Rights Under the ROFN, Option, and License Agreement

Section 2.1 Grant of Option and Option Exercise.

On April 1, 2023, Biogen exercised the Option under Section 2.2 of the ROFN, Option, and License Agreement for the ATV:Abeta Program, and Biogen was granted the licenses in Section 4.1 (Licenses to Biogen) for the ATV:Abeta Program. All rights and obligations of the Parties under the ROFN, Option, and License Agreement based on the Biogen's exercise of the Option for the ATV:Abeta Program will remain in full force and effect under the ROFN, Option, and License Agreement and is in all respects agreed to, ratified, and confirmed hereby.

As of the Amendment Effective Date, the Parties mutually agree that Biogen hereby irrevocably waives the Option, and Denali hereby terminates its grant to Biogen of the Option, under Section 2.2 of the ROFN, Option, and License Agreement to the Option TV Program, including without limitation any rights and obligations related thereto under the ROFN, Option, and License Agreement. In light of Denali's termination of its grant to Biogen of the Option with respect to the Option TV Program, Denali hereby directs Biogen to destroy all tangible items bearing, containing, or contained in, any of the Confidential Information of Denali that is related to the Option TV Program.

Section 2.2 Grant of ROFN.

As of the Amendment Effective Date, the Parties mutually agree that Biogen also hereby irrevocably waives all of Biogen's rights to the rights of first negotiation under Section 3.1.1 of the ROFN, Option, and License Agreement, including without limitation any rights to negotiate any ROFN Definitive Agreement with Denali, and Denali shall have no further obligations to Biogen under Article 3 of the ROFN, Option, and License Agreement, including without limitation to provide to Biogen any ROFN Initial Notice under Section 3.1.1 or ROFN Update Report under Section 3.2.2, or otherwise with respect to the ROFN Programs.

[***] Certain information in this document has been omitted from this exhibit because it is both (i) not material and (ii) would be competitively harmful if publicly disclosed.

In addition, SCHEDULE 1

FORM OF EXERCISE NOTICE

[To be executed by the definition Holder to purchase shares of "ROFN Term" in Section 1.242 Common Stock under the Warrant]

Ladies and Gentlemen:

(1) The undersigned is the Holder of Warrant No. __ (the "Warrant") issued by Denali Therapeutics Inc., a Delaware corporation (the "Company"). Capitalized terms used herein and not otherwise defined herein have the ROFN, Option, and License Agreement is hereby deleted, and in its place, the following is inserted: "'**ROFN Term**'means the period beginning on the Provisional Agreement Effective Date and expiring on the Amendment Effective Date."

In light of the termination of the ROFN, Option, and License Agreement with respect to all ROFN Programs as of the Amendment Effective Date, the terms of Section 14.6.2 of the ROFN, Option, and License Agreement shall apply. Denali hereby directs that Biogen destroy all tangible items bearing, containing, or contained in, any of the Confidential Information of Denali that is solely related to the ROFN Programs.

Section 2.3 Ratification and Confirmation of ROFN, Option, and License Agreement.

The ROFN, Option, and License Agreement, except where rights and obligations have been waived or the terms have been explicitly amended by this Amendment, will remain unchanged and in full force and effect and is in all respects agreed to, and are hereby ratified and confirmed. Any reference to the ROFN, Option, and License Agreement after the Amendment Effective Date will be deemed to be a reference to the ROFN, Option, and License Agreement, as amended by this Amendment.

Section 3. Entire Agreement.

This Amendment sets forth and constitutes the entire agreement and understanding between the Parties with respect to the subject matter hereof and all prior agreements, understandings, promises, and representations, whether written or oral, with respect thereto are superseded hereby. Each Party confirms that it is not relying on any representations or warranties of the other Party except as specifically respective meanings set forth in this Amendment. No amendment, modification, release, or discharge the Warrant.
(2) The undersigned hereby exercises its right to this Amendment purchase Warrant Shares pursuant to the Warrant.

(3) The Holder intends that payment of the Exercise Price shall be binding upon the Parties, unless in writing and duly executed by authorized representatives of both Parties. made as (check one):

[Signature Page Follows]

IN WITNESS WHEREOF, the Parties have caused this Amendment to be executed by their respective duly authorized officers.

Deal Therapeutics Inc.

By:

Name:

Title:

Biogen MA, Inc.

By:

Name:

Title:

☐ Cash Exercise

☐ "Cashless Exercise" under Section 10 of the Warrant

(4) If the Holder has elected a Cash Exercise, the Holder shall pay the sum of $ in immediately available funds to the Company in accordance with the terms of the Warrant.

(5) Pursuant to this Exercise Notice, the Company shall deliver to the Holder Warrant Shares determined in accordance with the terms of the Warrant.

(6) By its delivery of this Exercise Notice, the undersigned represents and warrants to the Company that in giving effect to the exercise evidenced hereby the Holder, together with the Attribution Parties, will not beneficially own in excess of the number of shares of Common Stock (as determined in accordance with Section 13(d) of the Securities Exchange Act of 1934, as amended) permitted to be owned under Section 11 of the Warrant to which this notice relates.

Dated: _____

Name of Holder: _____

By: _____

Name: _____

Title: _____

(Signature must conform in all respects to name of Holder as specified on the face of the Warrant)

SCHEDULE 2

ASSIGNMENT FORM

(To assign the foregoing Warrant, execute this form and supply required information. Do not use this form to purchase shares.)

FOR VALUE RECEIVED, the foregoing Warrant and all rights evidenced thereby are hereby assigned to

Name:

Biogen International GmbH

By:

Name:

Title:
(Please Print)

Address:

(Please Print)

Phone Number:
Email Address:
Dated: _____ __, _____
Holder's Signature:
Holder's Address:

[***] Certain information in this document has been omitted from this exhibit because it is both (i) not material and (ii) would be competitively harmful if publicly disclosed.

Exhibit A

Updated Global Development Plan/Budget

[***]

[***] Certain information in this document has been omitted from this exhibit because it is both (i) not material and (ii) would be competitively harmful if publicly disclosed.

Exhibit 31.1

CERTIFICATION OF PERIODIC REPORT UNDER SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Ryan J. Watts, Ph.D., certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Denali Therapeutics 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 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;

5. The registrant's other certifying officer 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: November 7, 2023 May 7, 2024

/s/ Ryan J. Watts

Ryan J. Watts, Ph.D.

President and Chief Executive Officer

rcumstances on which any statement is based. Contact InceptionGrowth Acquisition Limited Investor Relationship Department (315) 636-6638 {graphic omitted} {graphic omitted} mily:'Calibri',sans-serif;min-width:fit-content;">

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Exhibit 31.2

CERTIFICATION OF PERIODIC REPORT UNDER SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Alexander O. Schuth, M.D., certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Denali Therapeutics 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 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;

5. The registrant's other certifying officer 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: November 7, 2023 May 7, 2024

/s/ Alexander O. Schuth

Alexander O. Schuth, M.D.

Chief Operating and Financial Officer

ch any statement is based. Contact InceptionGrowth Acquisition Limited Investor Relationship Department (315) 636-6638 {graphic omitted} {graphic omitted} mily:'Calibri',sans-serif;min-width:fit-content;">

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Exhibit 32.1

CERTIFICATION OF CHIEF EXECUTIVE OFFICER
PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

Pursuant to the requirement set forth in Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended, (the "Exchange Act") and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. §1350), I, Ryan J. Watts, Ph.D., President and Chief Executive Officer of Denali Therapeutics Inc. (the "Company"), hereby certify that:

1. The Company's Quarterly Report on Form 10-Q for the fiscal period ended September 30, 2023 March 31, 2024, to which this Certification is attached as Exhibit 32.1 (the "Periodic Report"), fully complies with the requirements of Section 13(a) or Section 15(d) of the Exchange Act; and

2. The information contained in the Periodic Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: November 7, 2023 May 7, 2024

By:	/s/ Ryan J. Watts
Name:	Ryan J. Watts, Ph.D.
Title:	President and Chief Executive Officer

Exhibit 32.2

CERTIFICATION OF CHIEF FINANCIAL OFFICER
PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

Pursuant to the requirement set forth in Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended, (the "Exchange Act") and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. §1350), I, Alexander O. Schuth, M.D., Chief Operating and Financial Officer of Denali Therapeutics Inc. (the "Company"), hereby certify that:

1. The Company's Quarterly Report on Form 10-Q for the fiscal period ended September 30, 2023 March 31, 2024, to which this Certification is attached as Exhibit 32.2 (the "Periodic Report"), fully complies with the requirements of Section 13(a) or Section 15(d) of the Exchange Act; and

2. The information contained in the Periodic Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: November 7, 2023 May 7, 2024

By:	/s/ Alexander O. Schuth
Name:	Alexander O. Schuth, M.D.
Title:	Chief Operating and Financial Officer