First Quarter 2025 Results Call

Corporate Update & Financial Results

May 5, 2025

Forward-looking statements

BioCryst's presentation contains forward-looking statements, including, but not limited to, statements regarding future results and forward-looking financial information, company performance, achievements, future market share or size, and expectations regarding pipeline development. These statements are subject to known and unknown risks, uncertainties and other factors which may cause actual results, performance, achievements, market share or size, or pipeline development outcomes to be materially different from any future results, performance, achievements, market share or size, or pipeline development expectations expressed or implied in this presentation. These statements reflect our current belief with respect to future events and are based on assumptions and are subject to risks and uncertainties. In addition, the outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results.

You should not place undue reliance on the forward-looking statements. For additional information, including important risk factors, please refer to BioCryst's documents filed with the SEC and located at ir.biocryst.com/financial-information/sec-filings.

Non-GAAP Financial Measures

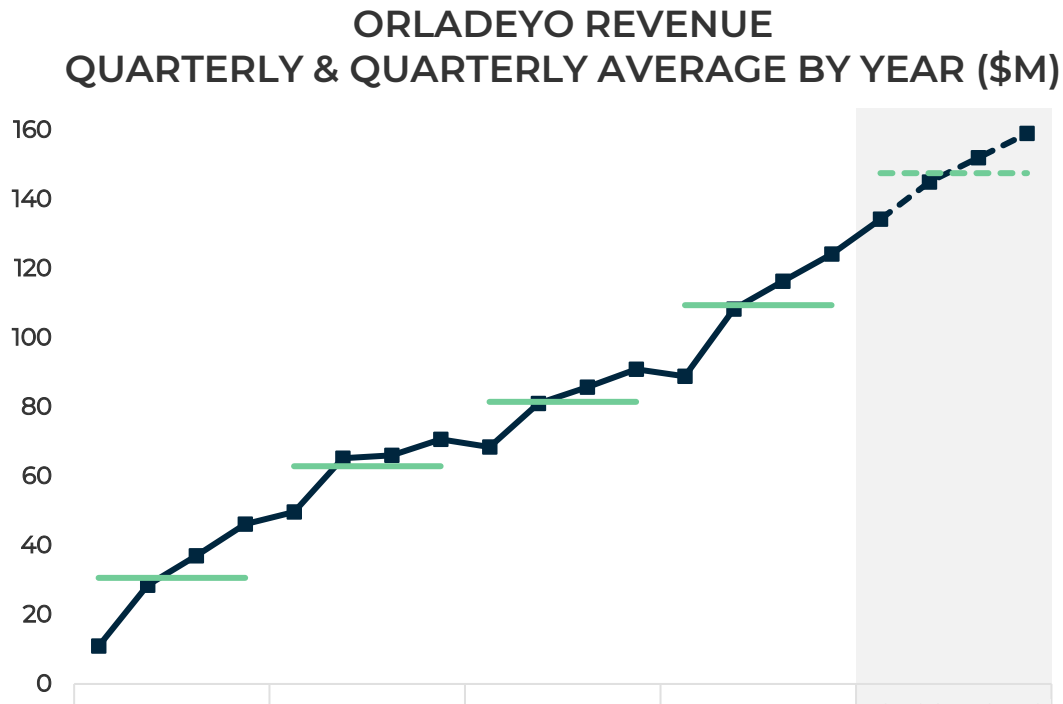
In addition to financial information prepared in accordance with U.S. GAAP, this presentation also includes our non-GAAP operating expense outlook for full year 2025, which refers to our expected GAAP operating expense, excluding stock-based compensation expense. We have not provided a reconciliation against the comparable forward-looking GAAP measure because we are unable to predict with reasonable certainty the full amount of stock-based compensation expense for full year 2025 without unreasonable effort. Stock-based compensation expense is uncertain and depends on various factors, including our future hiring and retention needs, as well as the future fair market value of our common stock, which is difficult to predict and subject to change. The actual amount of stock-based compensation expense for the full year 2025 could have a material impact on GAAP reported results for the guidance period.

AGENDA

Corporate update	**Jon Stonehouse** President and Chief Executive Officer
ORLADEYO® update	**Charlie Gayer** Chief Commercial Officer
Pipeline update	**Dr. Helen Thackray** Chief Research and Development Officer
Financial update	**Jon Stonehouse** President and Chief Executive Officer
Q&A	

BioCryst: durable, profitable growth through the decade with pipeline optionality

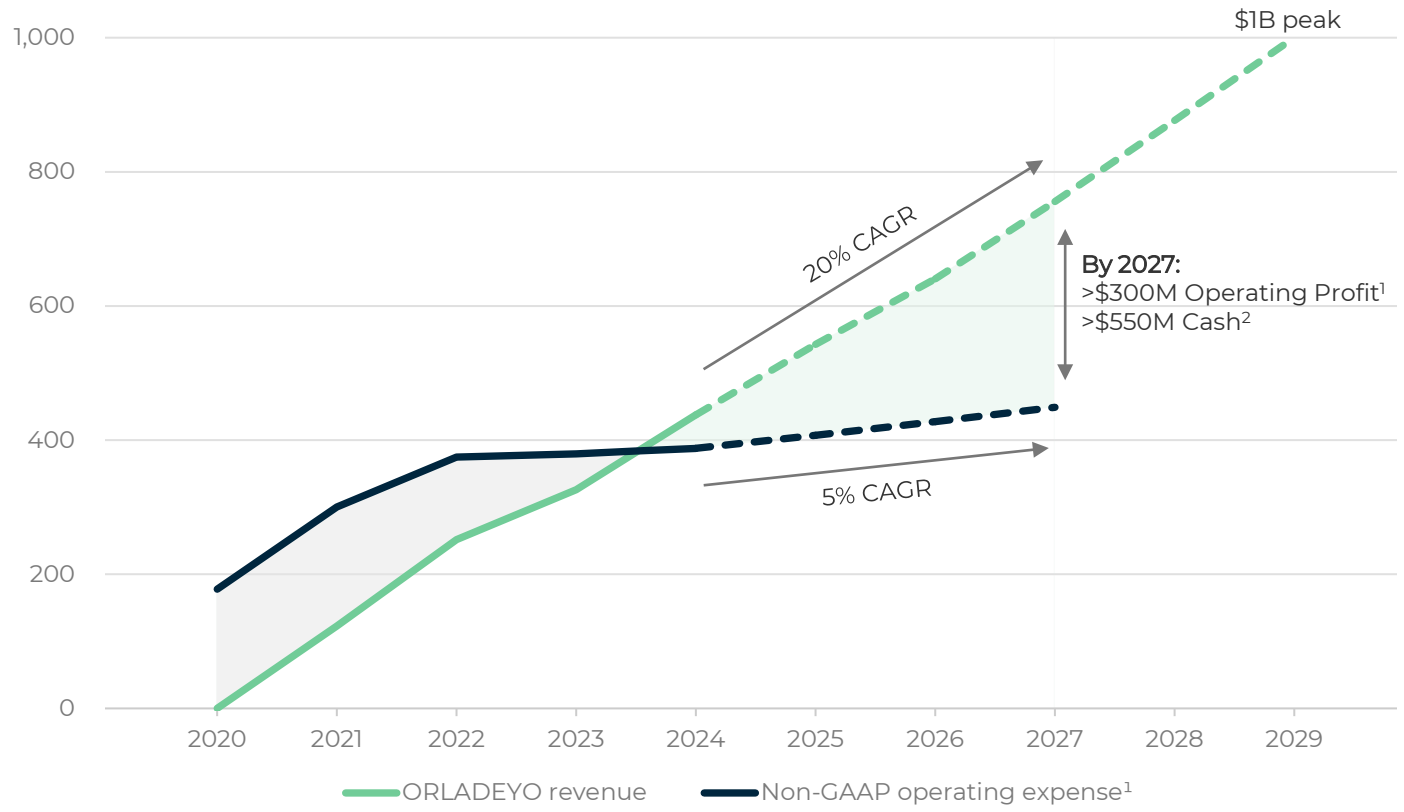
Excellent Q1 ORLADEYO result sets up FY 2025 for record year



	2021	2022	2023	2024	2025 Guidance
Revenue ($M)	123	252	326	438	580-600
Growth ($M)	+123	+129	+74	+112	+142-162
Growth (%)	–	+105%	+29%	+34%	+33-37%

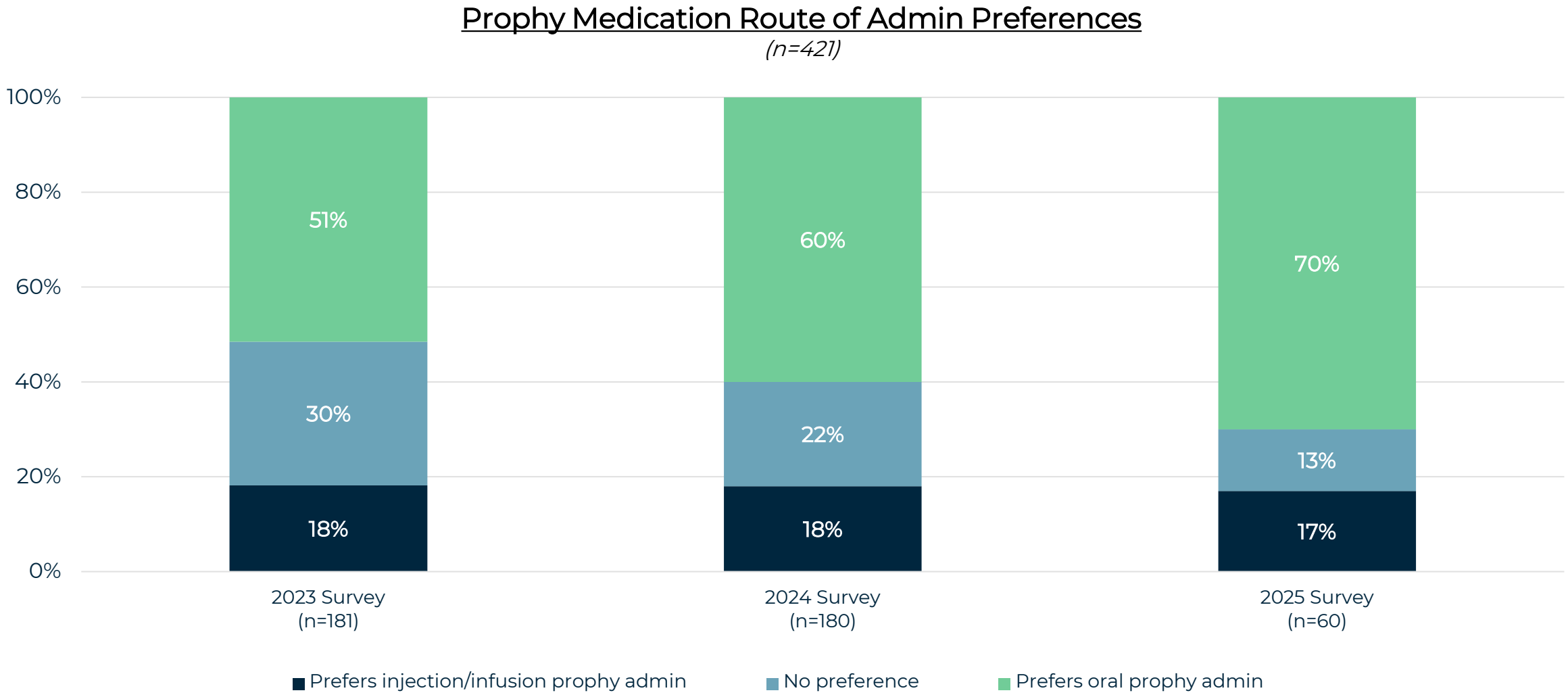
- Better-than-expected commercial execution in Q1
  - ~84% paid rate across all patients
  - More revenue captured during reauthorizations
  - Revenue will flow through the full year as a result
  - Q1-to-Q2 revenue jump will reflect smoother quarterly cadence
- Strong underlying demand remains consistent with 2024
- FY 2025 guidance raised to $580-600M (+33-37% growth)

ORLADEYO growth + focused capital allocation to drive sustained profitability



1. Not including stock-based compensation
2. Includes impact from debt paydown of $75M in April 2025

MARKET RESEARCH: Patient preference for an oral route of administration for HAE LTP has increased steadily year over year since 2023



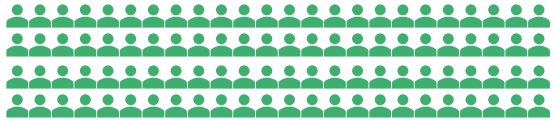
Source: BioCryst Internal Market Research Survey (Quarterly 2023-24, Q1 2025)
LTP = long-term prophylaxis

Comprehensive annual research + market simulation

OUR MODEL STARTS WITH PREFERENCE AND SIMULATES 6,000 MARKET INTERACTIONS BETWEEN HCPS, PATIENTS, & PAYERS

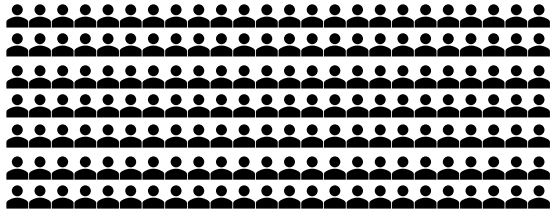
Research Sample*

PATIENTS



n=100 HAE patients

PHYSICIANS



*n=100 AIs**, and n=75 non-AIs***

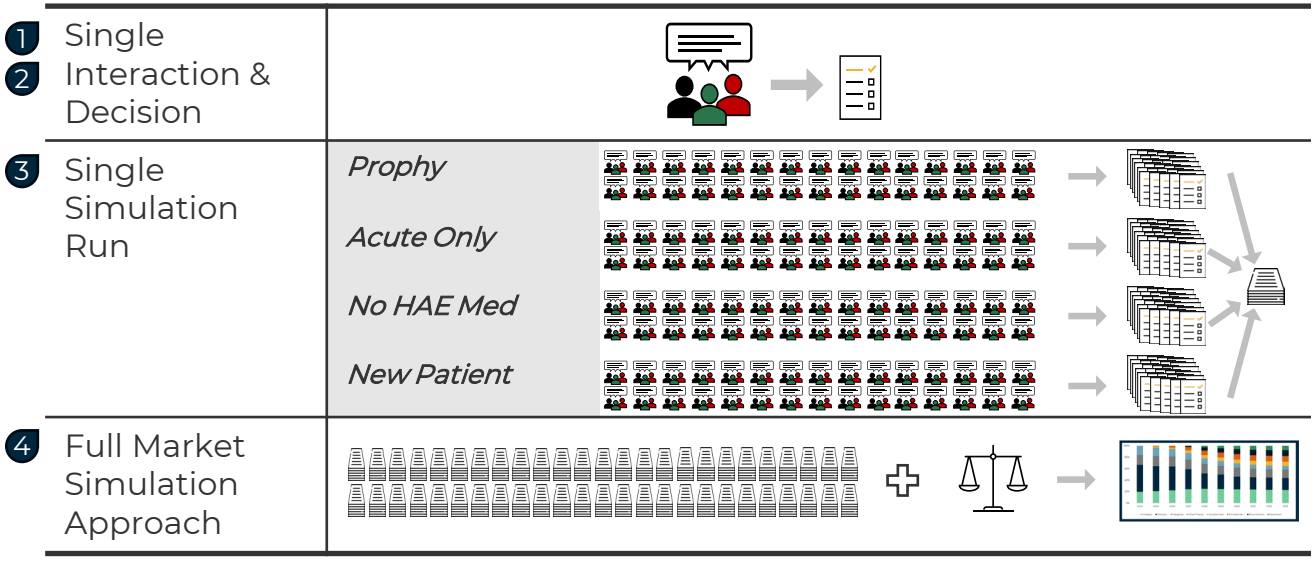
PAYERS

n=56 decision makers covering over 200 million total lives.

Market Model Simulation (Monte Carlo)

1. A patient, physician, and payer are randomly selected from survey respondents.
2. The model evaluates individual prescribing decisions based on patient preference, physician preference & payer approval within a framework of market dynamics (e.g., awareness, adoption, launch timing)
3. For a single simulation run, the process is repeated 30 times for each patient category
4. The simulation is then repeated 50 times (6,000 interactions) to create a generalized distribution, then scaled and weighted to HAE total population

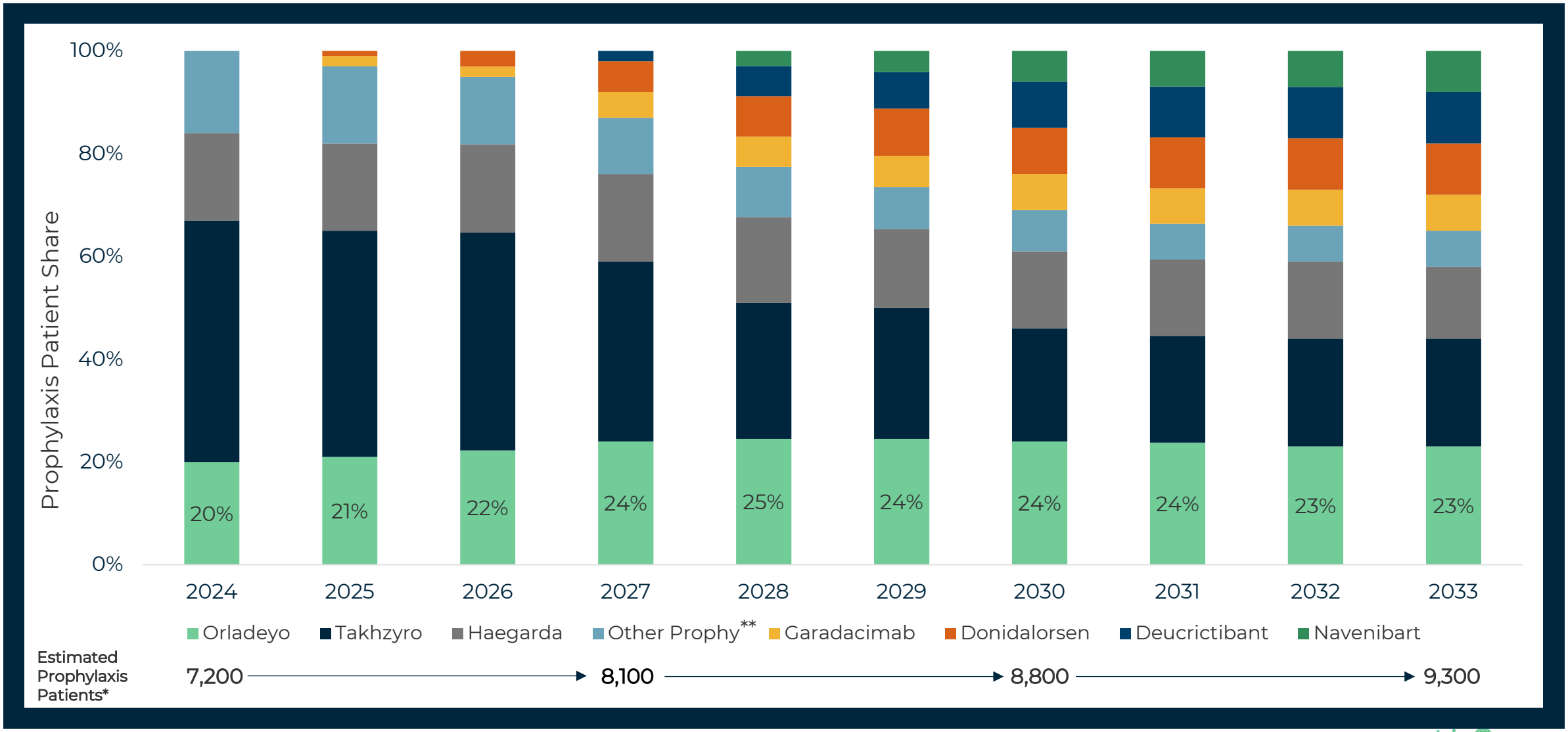
Modeling Process - Visual Example



* Choice-based conjoint
** HAE treaters: Allergists & Immunologists

Monte Carlo simulation outcome: U.S. prophy market share

ORLADEYO REACHES A STEADY STATE OF OVER 2,000 PATIENTS IN U.S. DURING 2028, EVEN AS NEW PRODUCTS GAIN SHARE



Source: BioCryst Internal Market Research Study (Conducted Jun 2024) *Source: 2018-2023 administrative claims data
**Other Prophy: Any other current medication (including acute) taken prophylactically for HAE

Our pipeline

ASSET	PROGRAM	LEAD OPTIMIZATION	PRE-CLINICAL	PROOF OF CONCEPT†	PIVOTAL‡	APPROVED / COMMERCIAL
ORLADEYO® (berotralstat) Oral Plasma Kallikrein Inhibitor	Hereditary Angioedema (HAE)					
ORLADEYO® (berotralstat) Oral Plasma Kallikrein Inhibitor (age ≥2 years)	Hereditary Angioedema (HAE)					
BCX17725 Protein Therapeutic	Netherton Syndrome					
Avoralstat Ocular Plasma Kallikrein Inhibitor	Diabetic Macular Edema (DME)					
Oral C5 Inhibitor	Complement-Mediated Diseases					
Oral C2 Inhibitor	Complement-Mediated Diseases					
Bifunctional Complement Inhibitor	Complement-Mediated Diseases					

**ORLADEYO (age ≥ 2 years), BCX17725, and avoralstat are investigational and have not been deemed safe and effective by the FDA.*

†Proof of Concept is typically Phase 1 or 2.

‡Pivotal is typically Phase 3.

This is BIG: bringing ORLADEYO to children

- Despite significant innovation in HAE prophylaxis for adults, there is still high unmet need in children
- Injectable therapies are the only FDA-approved options for children ages 2 to 11
- Positions ORLADEYO to be the market leading prophylaxis for children (~500 patients in US)

New dosage form: granules (2x3 mm)

APeX-P

- Ages 2 to 11
- Multi-center pivotal trial
- Primary outcomes were safety and exposure levels in pediatric patients with HAE

US NDA Submitted

Additional 2025 Submissions: EU, Japan, Canada

Treating Netherton syndrome (NS) with a targeted KLK5 inhibitor: BCX17725

High unmet need

Severe, rare, genetic and lifelong disease

Premature separation of skin layers, severe inflammation and infection risk

No approved targeted therapies

Validated target

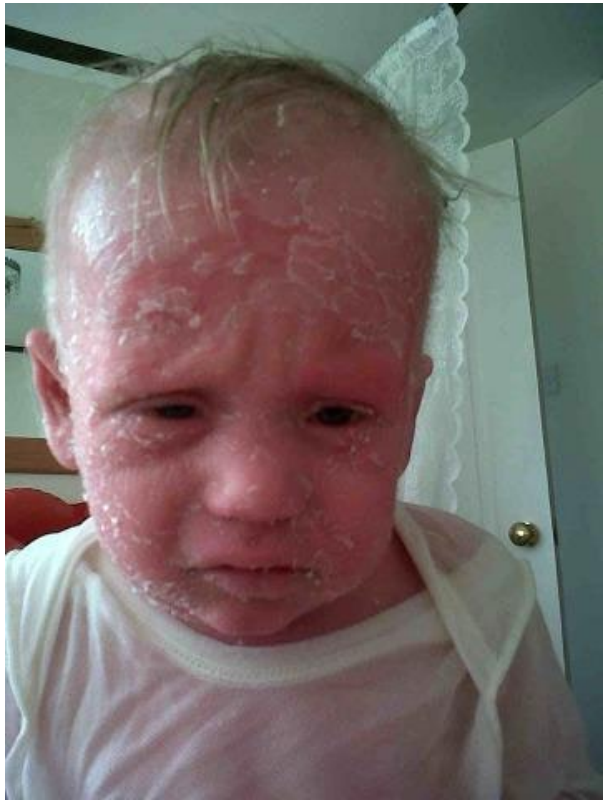
Well-understood biological cause: mutation in *SPINK5* gene

BCX17725 replaces missing protein functions

Under-diagnosed population

Diagnosed US population of ~1,600[1]

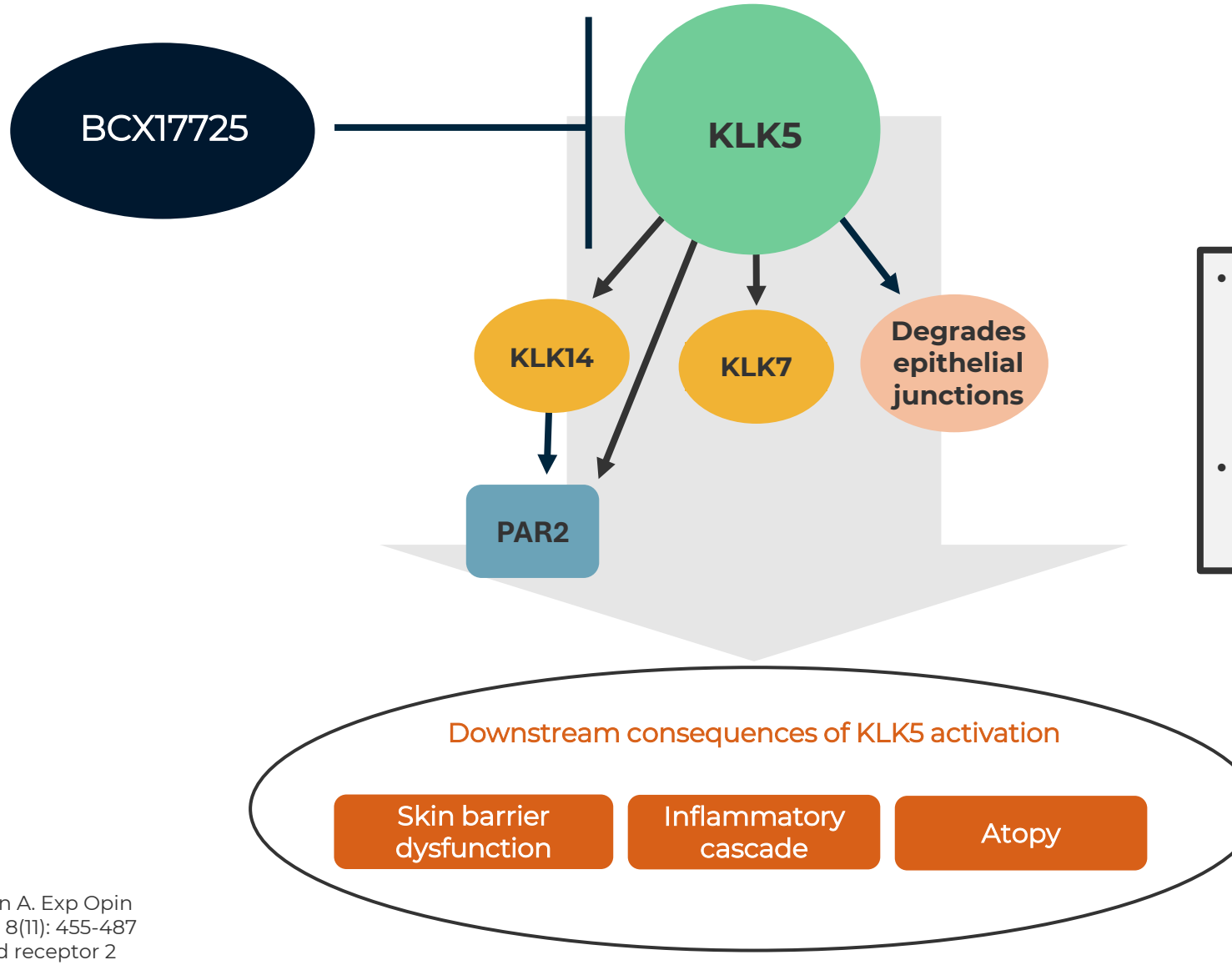
Potential to grow to 3,000-5,000 with greater diagnosis and treatment



IND cleared by FDA

1. Based on healthcare claims analysis
Image: https://www.nethertonsyndrome.com/about-nethertons.php

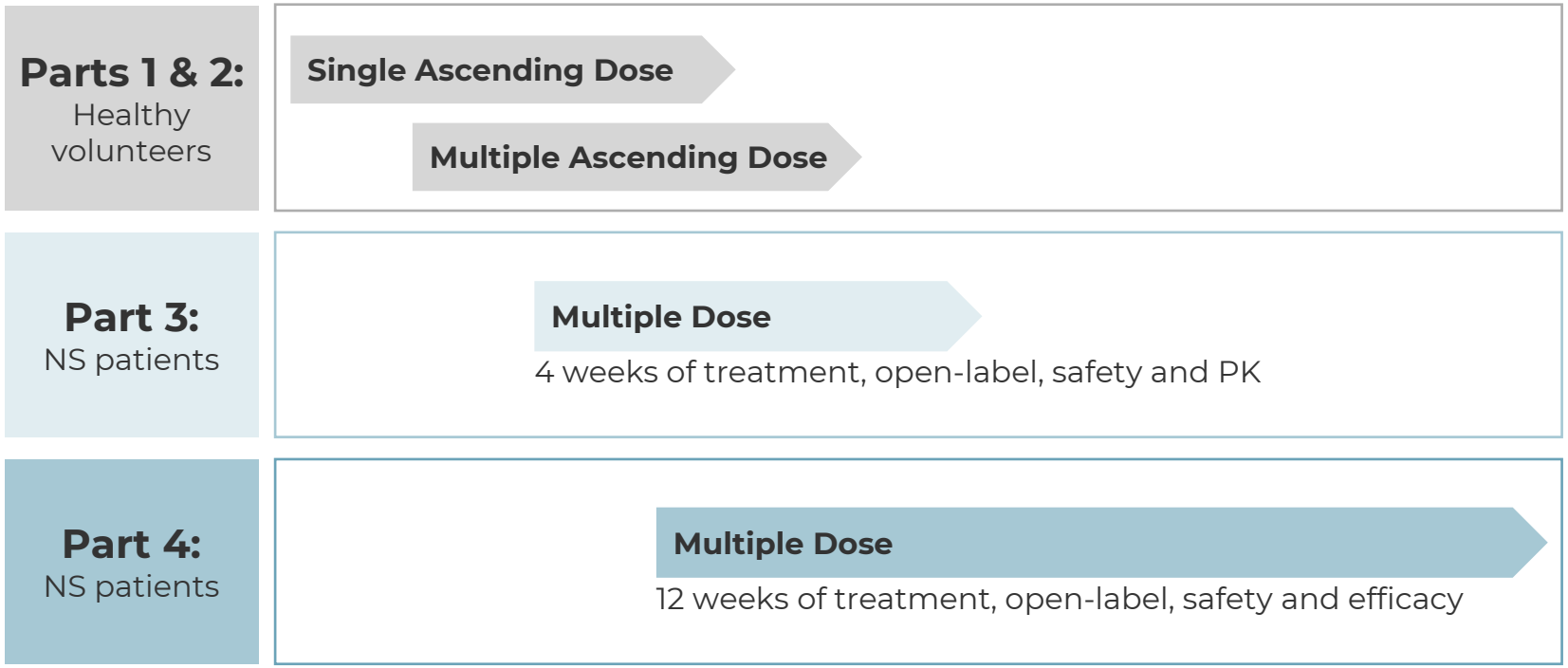
BCX17725 targets KLK5, the key player in Netherton syndrome



- KLK5 initiates the pathologic protease cascade (KLK7, KLK14) and inflammation (via PAR2) in the skin
- BCX17725 designed to stop KLK5 overactivity at the top of the pathway

Petrova E and Hovnanian A. Exp Opin Orphan Drugs (2020) 8(11): 455-487
PAR2: protease-activated receptor 2
KLK = kallikrein

BCX17725 Phase 1: healthy volunteers and patients with Netherton syndrome



Potential early signals from measures of:

- IGA
- KLK5 activity in skin
- IASI (Part 4)
- TEWL

IGA: Investigator's Global Assessment scale
IASI: Ichthyosis Area and Severity Index
TEWL: Transepidermal Water Loss

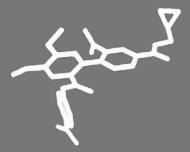
Addressing DME with a potent plasma kallikrein inhibitor: avoralstat suprachoroidal injection[1]

Alternative MOA

Compelling evidence for plasma kallikrein activity in DME pathobiology

New options are needed: up to 40% of patients have persistent DME despite anti-VEGF treatment

Right drug + delivery



High potency and low solubility/depot effect are attractive for ophthalmic dosing

Potential for disease modifying outcomes + extended dosing interval

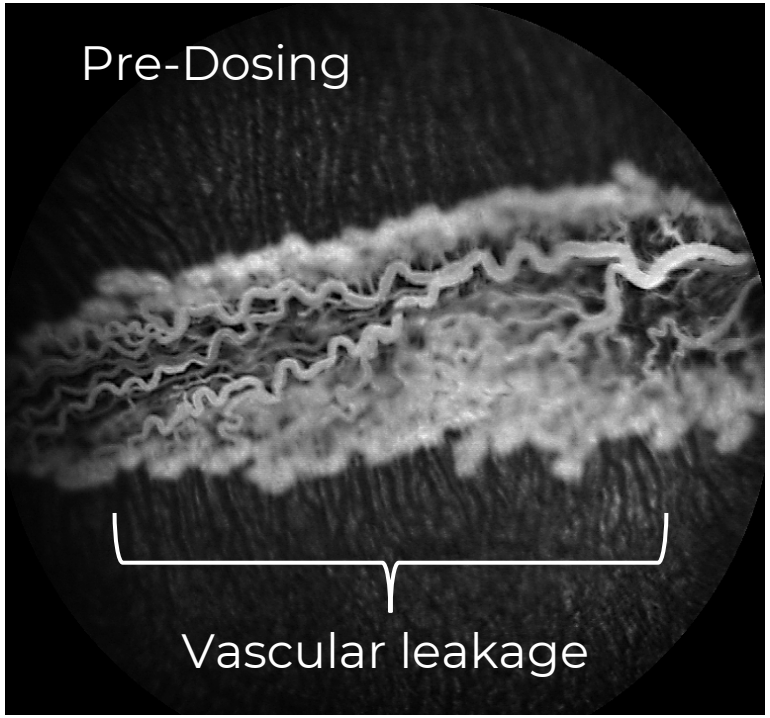
Significant market opportunity

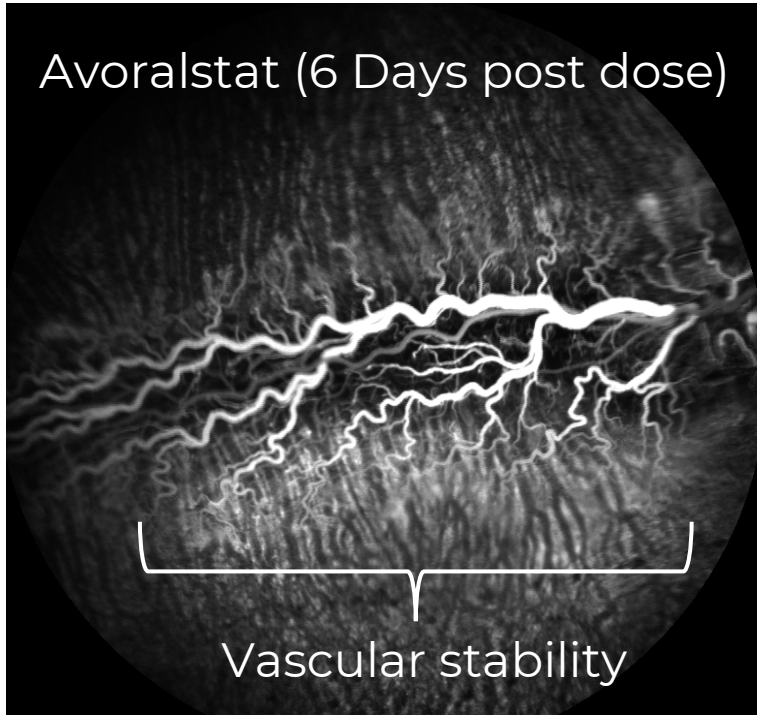
~1.5M DME patients in US

Est. $4B VEGF market by 2028

1. SCS Microinjector® is licensed from Clearside Biomedical, Inc.; SCS, suprachoroidal space

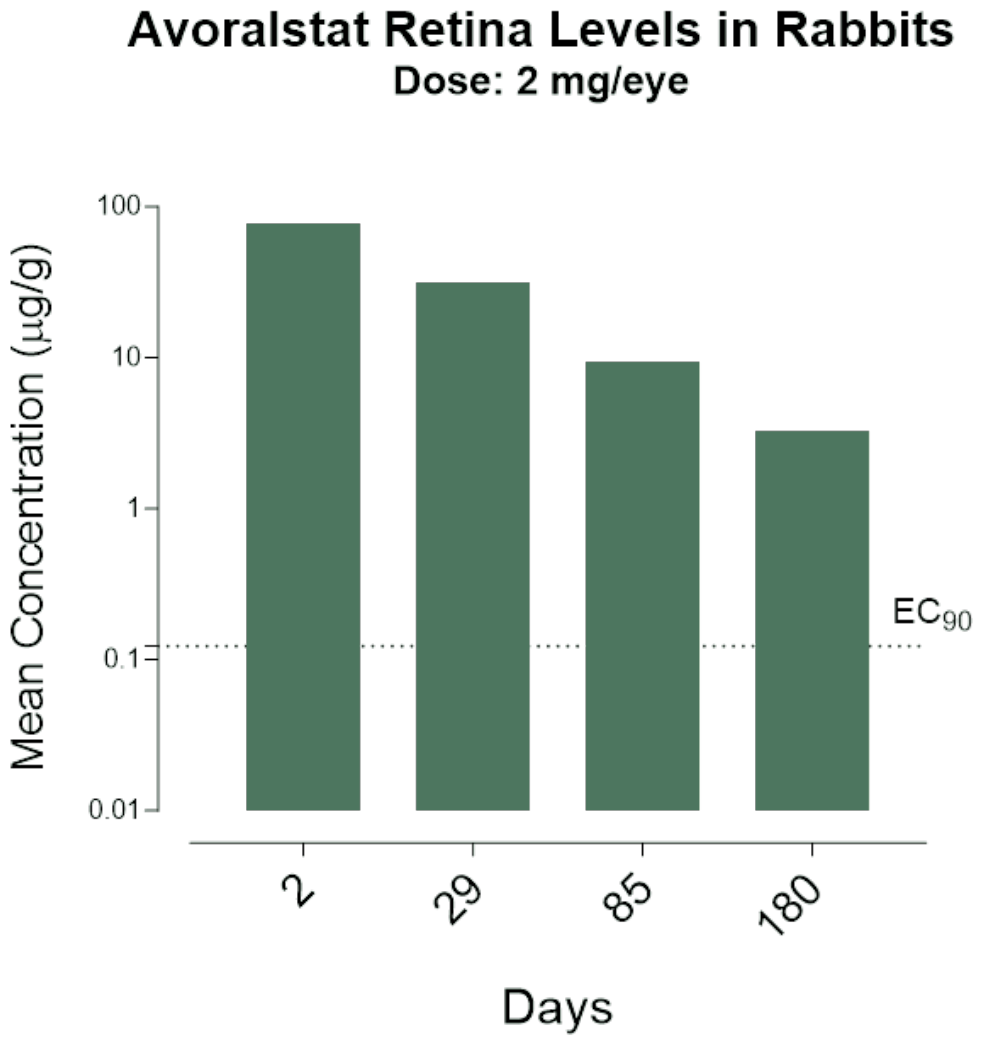
Preclinical evidence demonstrates plasma kallikrein pathway may reduce vascular leakage





Source: BioCryst Pharmaceuticals nonclinical data on file 2025., Kumar et al. Int J Ophthalmol. 2022 Jan 18;15(1):15-22
This slide shows a reduction of vascular leakage at 6 days post-treatment. This effect lasted through 21 days before leaking started to return by the next timepoint at day 36.

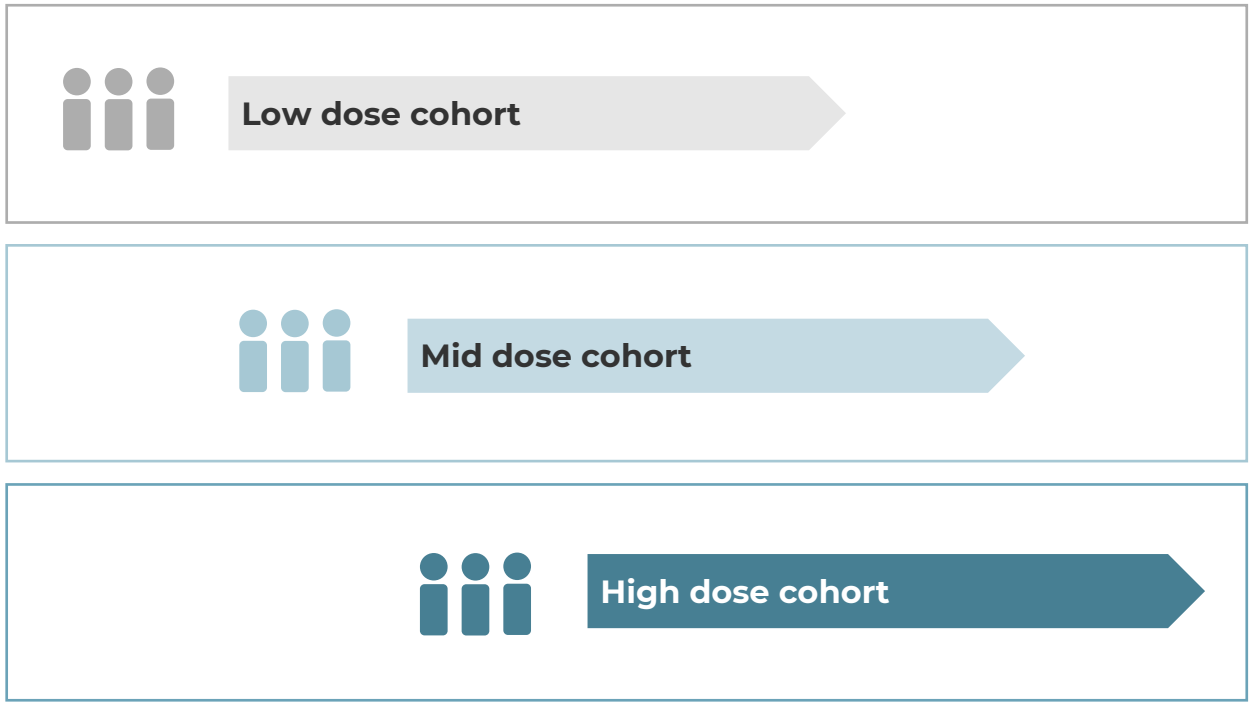
Suprachoroidal injection leads to 3+ months of sustained avoralstat levels in the retina[1]



1. BioCryst Pharmaceuticals nonclinical data on file 2025

This slide shows preclinical results, and the outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials.

Avoralstat Phase 1: patients with DME



- **Single dose**
- **24-week follow-up**
- **Data collected every 4 weeks**
  - Safety
  - Central subfield thickness
  - BCVA
- **Enrollment:**
  - Newly diagnosed patients
  - Patients previously treated with anti-VEGF

BCVA: best corrected visual acuity

Path to profitability significantly accelerated

2024

Full year operating profit[1]

2025
~~**2026**~~

Achieve positive net income & cash flows [2]

2026+

Meaningful & sustainable cash generation

1. Not including stock-based compensation
2. This positive cash flow is the improvement in cash, cash equivalents, restricted cash and investments from year end 2024 to year end 2025, not including the impact of the $75 million Pharmakon prepayment made in April 2025.

Key milestones in 2025

ORLADEYO revenue advances to royalty-free tier (>$550M)

Pediatric NDA for ORLADEYO

Initial BCX17725 and avoralstat clinical data

Accelerated full-year profitability

Finance summary

(Figures in millions)

Q1 2025 CASH POSITION	
Cash, cash equivalents, restricted cash & investments at December 31, 2024	$343
Cash, cash equivalents, restricted cash & investments at March 31, 2025	$317
Senior credit facility[1]	$324

PRO FORMA Q1 2025 CASH POSITION (ADJUSTED FOR DEBT PAYDOWN[2])	
Cash, cash equivalents, restricted cash & investments at Mar 31, 2025	$240
Senior credit facility	$249

2025 FY GUIDANCE	PRIOR	CURRENT
ORLADEYO revenue	$535-550	$580-600
Non-GAAP operating expense (not including stock-based compensation)	$425-435	$440-450

1. From Pharmakon Advisors, $300M drawn at issuance in Q2 2023. The $324M balance above represents $300M initial issuance plus PIK interest.
2. In April 2025, the company paid down $75 million of the outstanding balance plus prepayment penalty.

Traditional debt and royalty breakdown (Q1'25)

Does not include subsequent paydown of $75 million

	March 31, 2025	December 31, 2024
Royalty financing obligations - current	34,305	32,676
Royalty financing obligations - long-term	466,613	481,053
Total royalty financing obligations	500,918	513,729
Secured term loan[2]	315,413	314,869

	Traditional Debt	Commercial Royalty
Initial amount	$300M term loan	$425M royalty upfronts
Partner(s)	Pharmakon (2023)	RP (2020, 2021)[1] OMERS (2021)[1]
Description	• Rate: 3 mo. SOFR +7.00% (With PIK option: +7.25%) • Maturity: April 2028 bullet • Financial covenants: None • PIK option: 50% of interest for first six quarters	• Non-recourse (payments funded with revenues) • Considered a "debt instrument" per GAAP • An effective interest rate is calculated based on forecasted royalties, which determines interest expense • Current balance = prior balance + interest expense – royalty paid • If interest expense > royalties paid, balance increases • If royalties paid > interest expense, balance decreases

1. Royalty terms described on next slide
2. Amortization of debt fees and issuance costs continues through expected life of deal (Q2'28)

Royalty obligations: terms

	Upfront	Product	Rate Tiers (Key Territories[2])	Rate Tiers (Other Markets[2])	Cumulative Payback Cap
RP 2020	$125M	ORLADEYO	$0-350M: 8.75% $350M-550M: 2.75% Over $550M: None	$0-150M: 20% $150M-230M: 10% Over $230M: None	None
RP 2021	$150M[1]	ORLADEYO	$0-350M: 0.75% $350M-550M: 1.75% Over $550M: None	$0-150M: 3% $150M-230M: 2% Over $230M: None	None
OMERS 2021	$150M	ORLADEYO	$0-350M: 10% $350M-550M: 3% Over $550M: None	$0-150M: 20% $150M-230M: 10% Over $230M: None	1.55x

1. Royalty Pharma made an additional $50M equity investment in conjunction with the 2021 Royalty Purchase Agreement
2. "Key Territories" include the United States, key European markets and other markets where ORLADEYO is sold directly or through distributors. "Other Markets" include revenue from licensees outside the Key Territories.

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