

BioCryst Pharmaceuticals, Inc.

Corporate Presentation

January 2025



Forward-looking statements

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



2024 highlights and 2025 outlook

COMMERCIAL EXCELLENCE

- **2024 Results:** \$437M global ORLADEYO® revenue (34% growth) and \$450M total revenue
- Over 1,200 US prescribers
- Commercially available in over 30 countries

CLINICAL PROGRESS

- ORLADEYO pediatric program on track for regulatory submission in 2025
- BCX17725 (Netherton syndrome) and avoralstat (DME) advancing into patients in 2025

BUILDING SUSTAINABLE PROFITABILITY

- Achieved goal for full-year 2024 operating profit¹
- On track for sustainable quarterly positive EPS and cash flow in 2H25
- Revenue expected to grow at ~20% CAGR over next 3 years, vs. ~5% for operating expenses

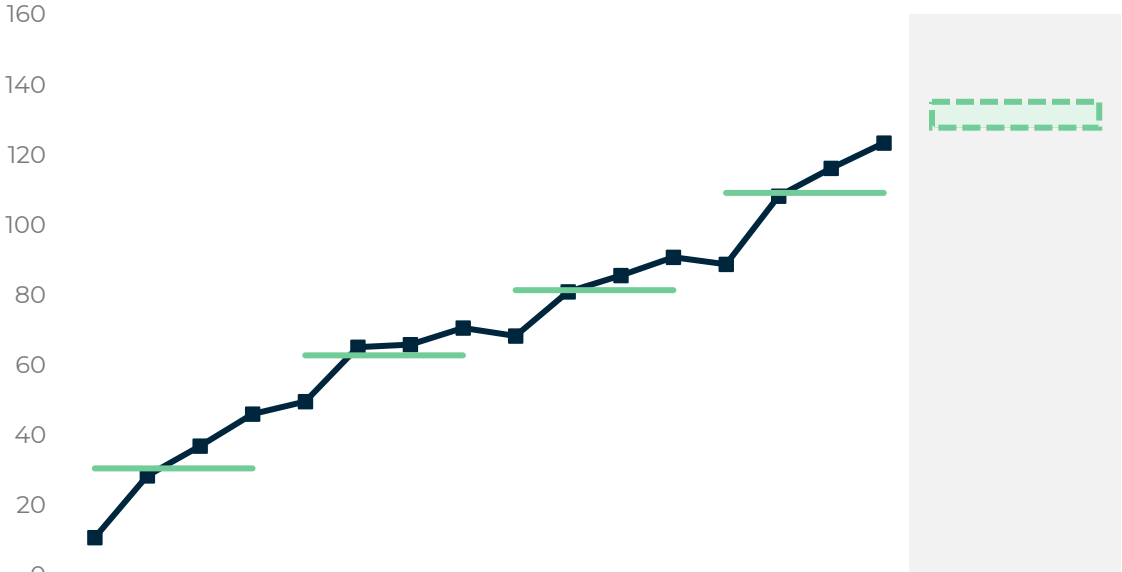
2025 REVENUE GUIDANCE

- **ORLADEYO:** \$515-535M
- **Total revenue:** \$540-560M

1. Excluding stock-based compensation expense

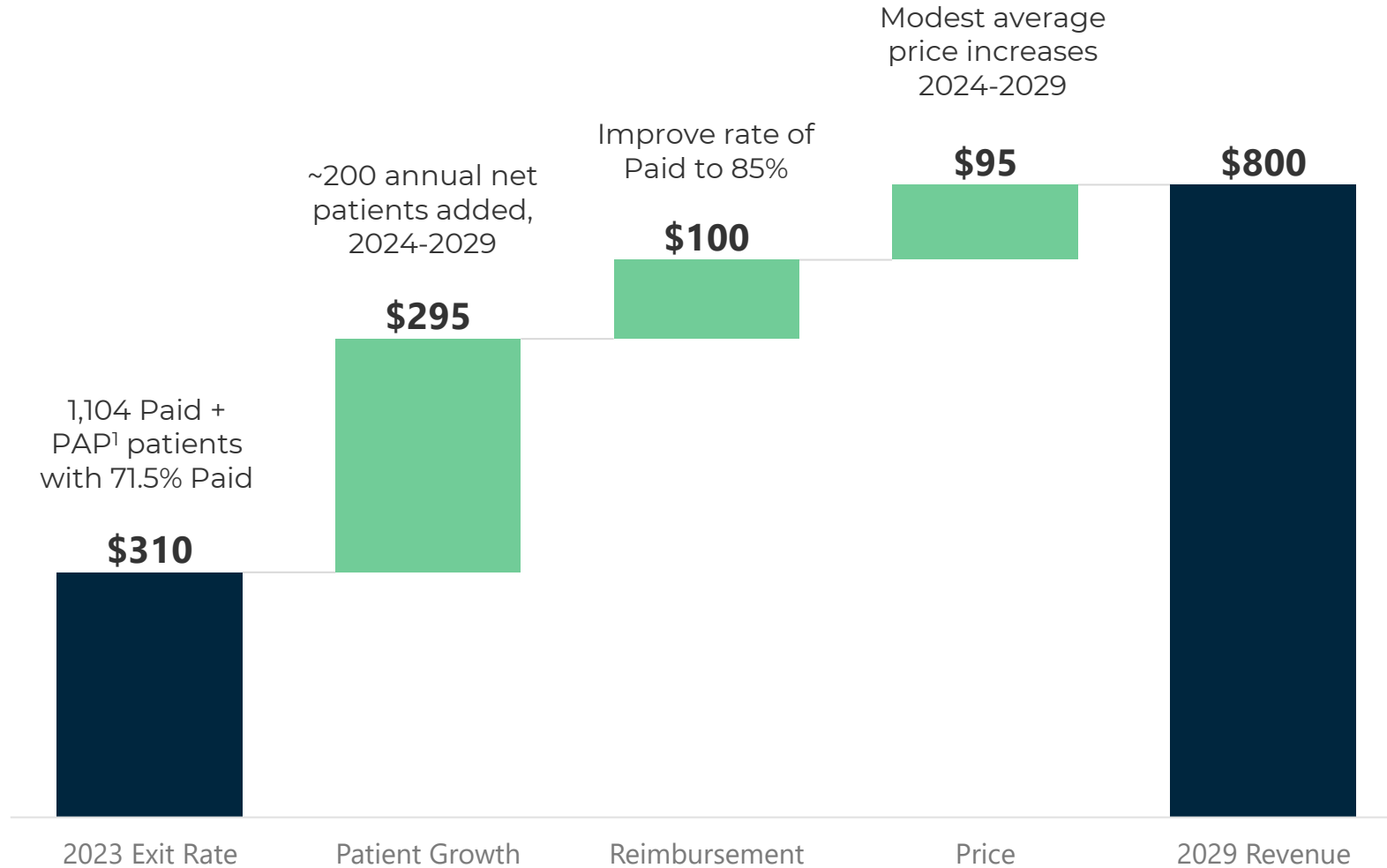
Strong ORLADEYO growth to continue in 2025

ORLADEYO REVENUE
QUARTERLY & QUARTERLY AVERAGE BY YEAR (\$M)



	1Q	2Q	3Q	4Q	1Q	2Q	3Q	4Q	1Q	2Q	3Q	4Q	1Q	2Q	3Q	4Q	1Q	2Q	3Q	4Q		
	2021				2022				2023				2024				2025 Guidance					
Revenue (\$M)																						
Growth (\$M)																						
Growth (%)																						

Path to \$800M US revenue in 2029



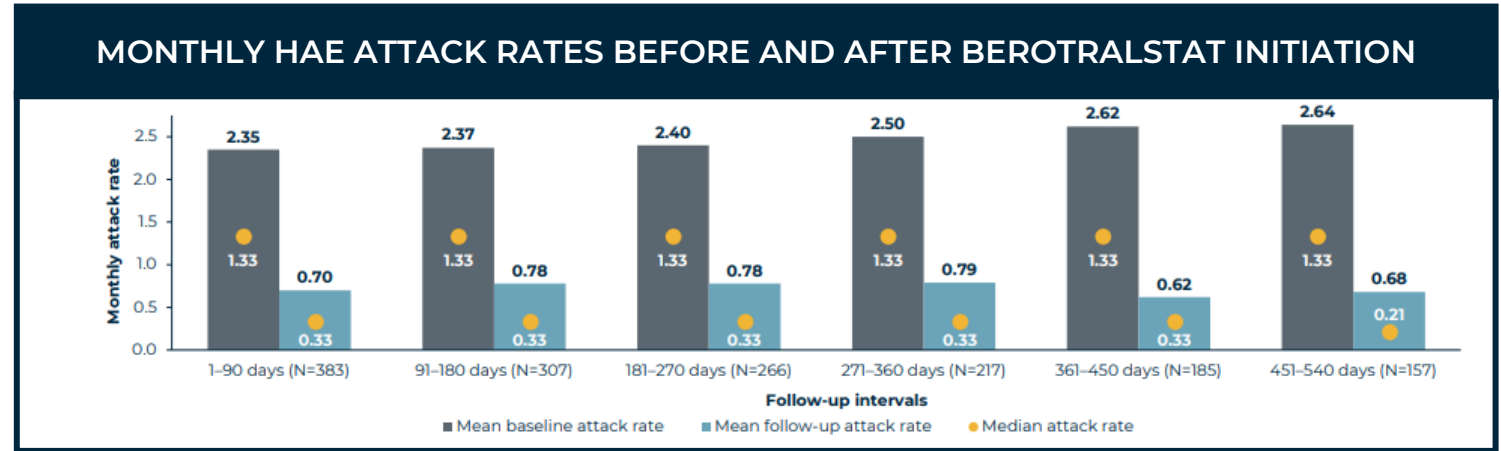
ASSUMPTIONS

- 15-20% gross-to-net on Paid shipments
- Compliance in low-90s%

1. PAP is the company's long-term patient assistance program

REAL WORLD EVIDENCE: patients with HAE Type 1 and 2 have significant and sustained attack reduction on ORLADEYO

- Median attack rate of 1/3rd of an attack per month in a study population of over 450 patients



Sustained Real-World Attack Reductions Following Berotralstat Initiation Among Patients with Hereditary Angioedema with C1-Inhibitor Deficiency

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INTRODUCTION

Hereditary angioedema (HAE) is a rare and potentially fatal disease characterized by recurrent and unpredictable attacks of laryngeal and/or subcutaneous swelling. The only available study evaluated and compared self-reported HAE attacks before and after initiation of berotralstat among patients with C1-inhibitor deficiency HAE type 1 and 2.

METHODS

This retrospective real-world study used data from Optima Specialty Pharmacy, the sole dispenser of berotralstat in the US, from December 15, 2020, to January 9, 2024.

RESULTS

The study population consisted of 466 patients with HAE type 1/2 with ≥2 berotralstat dispensings and ≥1 attack report at baseline and follow-up. The mean age was 40 years, most patients were female (82%), and nearly half of patients resided in the South (Table 1). Patients had significantly fewer HAE attacks after berotralstat initiation during each 90-day follow-up interval (0.62-0.79 attacks/month) versus baseline (2.35-2.64 attacks/month) (Figure 4).

Mean monthly attack rate reduction (95% CI) was 1.71 (1.26, 2.16) at 12 months in 271-360 day interval and 1.96 (1.40, 2.52) at 18 months in 451-540 day interval both p<0.0001 (Figure 4).

Figure 1. Monthly HAE Attack Rates (Mean and Median) Before and After Berotralstat Initiation

Figure 2. Eligibility Criteria and Patient Disposition

466 patients were included in the study. 113 patients were excluded: 47 for independent dispensing for berotralstat between baseline date and follow-up date, 66 for patients with only berotralstat dispensing, and 100 for patients with ≥2 berotralstat dispensings after baseline.

Table 1. Demographics and Clinical Characteristics

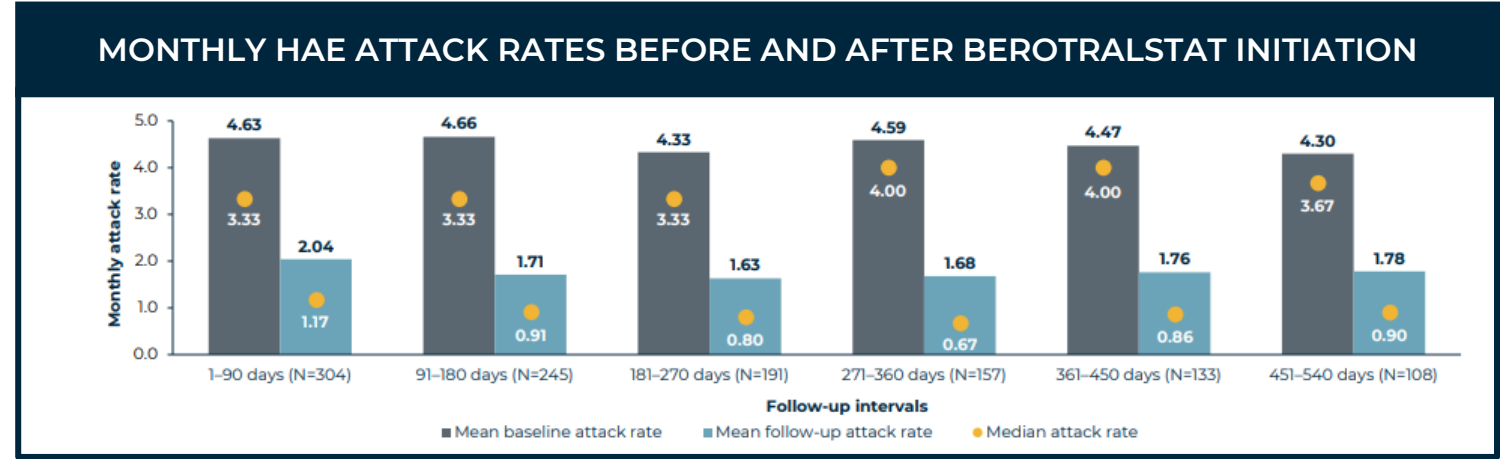
Characteristic	Patients (N=466)	n (%)
Demographics		
Age, mean ± SD (range), years	40.3 ± 16.2 (20)	
Female, n (%)	298 (63.9)	
Geographic region, n (%)		
North	109 (23.2)	
Midwest	74 (15.9)	
South	219 (46.8)	
West	64 (13.7)	
HAE Specialty, n (%)		
Type 1	112 (24.0)	
Type 2	254 (54.0)	
Unknown	100 (21.4)	

- The primary reason for reduced patient counts over time was that patients had not been on ORLADEYO long enough to be evaluated at all time points
- Only 68 (14.6%) out of 466 patients in this study discontinued therapy

Source: Sustained Real-World Attack Reductions Following Berotralstat Initiation Among Patients with Hereditary Angioedema with C1-Inhibitor Deficiency Presented at the ACAAI Scientific Meeting 2024 · October 24-28, 2024

REAL WORLD EVIDENCE: patients with HAE-nI-CI-inh have significant and sustained attack reduction on ORLADEYO

- Median attack rate of <1 per month in study population of over 350 patients
- Excellent attack reduction and control for a population that has struggled to find effective therapy



Sustained Real-World Attack Reductions Following Bertralstat Initiation Among Patients with Hereditary Angioedema without C1-Inhibitor Deficiency

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INTRODUCTION

- Hereditary angioedema (HAE) is characterized by recurrent and unpredictable attacks of subcutaneous and/or submucosal swelling, which can be life-threatening when affecting the upper airway.
- Some patients with HAE experience breakthrough-mediated angioedema despite normal plasma C1-inhibitor levels and function (HAE-nI-CI-inh).
- Bertralstat is a targeted once-daily oral medication for the prevention of HAE attacks in patients 12 years of age¹.
- This study evaluated and compared the real-world effectiveness of bertralstat on reducing self-reported HAE attacks among patients without C1-inhibitor deficiency (HAE-nI-CI-inh) in the US.

METHODS

- This retrospective real-world study used data from Optima Specialty Pharmacy, the rate dispenser of bertralstat in the US, from December 15, 2020, to January 6, 2024.
- The follow-up period commenced from the time that bertralstat dispensing data for the last bertralstat dispensing date; no patient assessment data were collected after the last bertralstat dispensing (Figure 1).

RESULTS

The study population consisted of 353 patients with HAE-nI-CI-inh with 12 bertralstat dispensing events and attack reports at baseline and follow-up (Figure 2).

The mean age was 48 years, most patients were female (76.2%), most patients resided in the Northeast (38.5%), and nearly half of patients resided in the South (Table 1).

Patients had significantly lower HAE attack rates when on bertralstat during each 90-day follow-up interval (3.33 attacks/month) versus baseline (4.59 attacks/month) (Figure 3).

Mean monthly attack rate reduction (95% CI) was 2.08 (1.47, 2.69) at 12 months (i.e., 271-360-day interval) and 2.53 (1.87, 3.19) at 18 months (i.e., 451-540-day interval) (Figure 4).

Table 1. Demographics and Clinical Characteristics

Characteristic	Patients (n/353)	Region	n (%)
Age, mean ± SD (median), years	48.1 ± 18.8 (49)	North	108 (30.6)
Female, n (%)	271 (76.2)	South	168 (47.6)
Patient weight, mean ± SD (median), kg	84 ± 22 (82)	Midwest	81 (23.0)
HCP specialty, n (%)	332 (94.4)	West	54 (15.3)
Allergist/immunologist	22 (6.3)	Northwest	42 (11.9)
Primary care physician	38 (10.8)	Unknown	6 (1.7)
Other	23 (6.5)		

CONCLUSION

Bertralstat was associated with statistically significant and sustained reductions in HAE attack rates through 18 months following bertralstat initiation among patients without C1-inhibitor deficiency in the US.

• The primary reason for reduced patient counts over time was that patients had not been on ORLADEYO long enough to be evaluated at all time points

• Only 75 (21.2%) out of 353 patients in this study discontinued therapy

Source: Sustained Real-World Attack Reductions Following Bertralstat Initiation Among Patients with Hereditary Angioedema without C1-Inhibitor Deficiency Presented at the ACAAI Scientific Meeting 2024 • October 24-28, 2024

Comprehensive annual research + market simulation

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

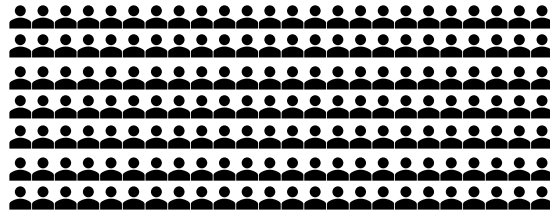
Research Sample*

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

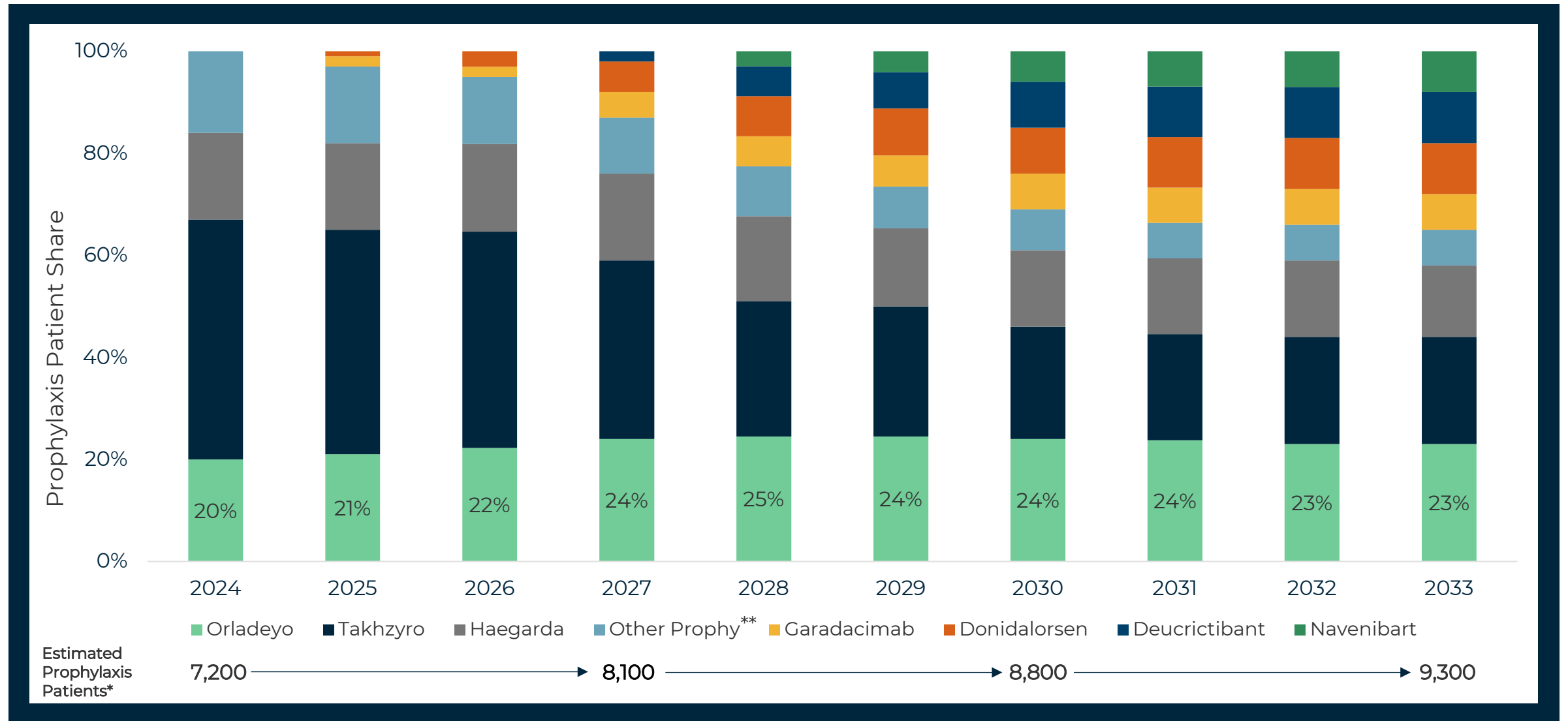
1	Single Interaction & Decision	
3	Single Simulation Run	<p><i>Prophy</i></p> <p><i>Acute Only</i></p> <p><i>No HAE Med</i></p> <p><i>New Patient</i></p>
4	Full Market Simulation Approach	

* Choice-based conjoint

** HAE treaters: Allergists & Immunologists

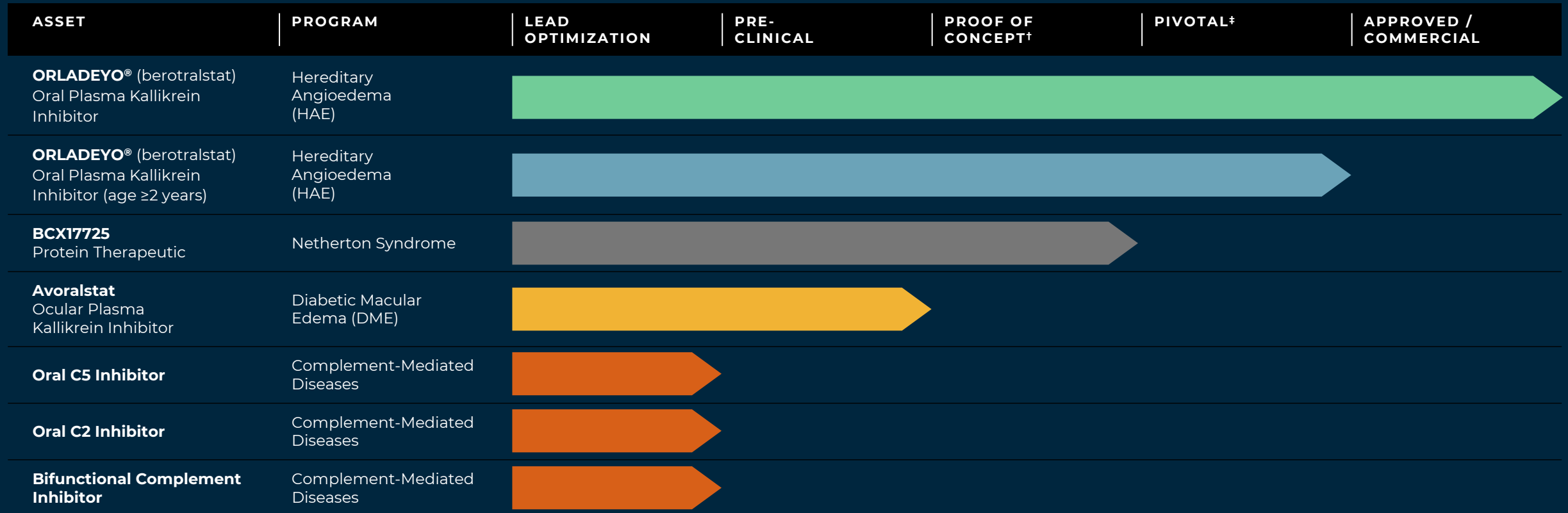
Monte Carlo simulation outcome: U.S. prophylaxis market share

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 Prophylaxis: Any other current medication (including acute) taken prophylactically for HAE

Our pipeline



*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 <12
- 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 <12
- Open label, multi-center
- Safety & PK study
- Analysis completed - submission planning underway

On track for NDA filing in 2025

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

**High
unmet
need**



Severe, rare, genetic and lifelong disease with no approved targeted therapies

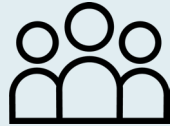
**Validated
target**



Well-understood biological cause:
mutation in SPINK5 gene

BCX17725 functionally replaces the
missing protein

**Under-
diagnosed
Population**



Diagnosed US population of ~1,600¹
with potential to grow to 3,000-
5,000 with greater diagnosis and
treatment

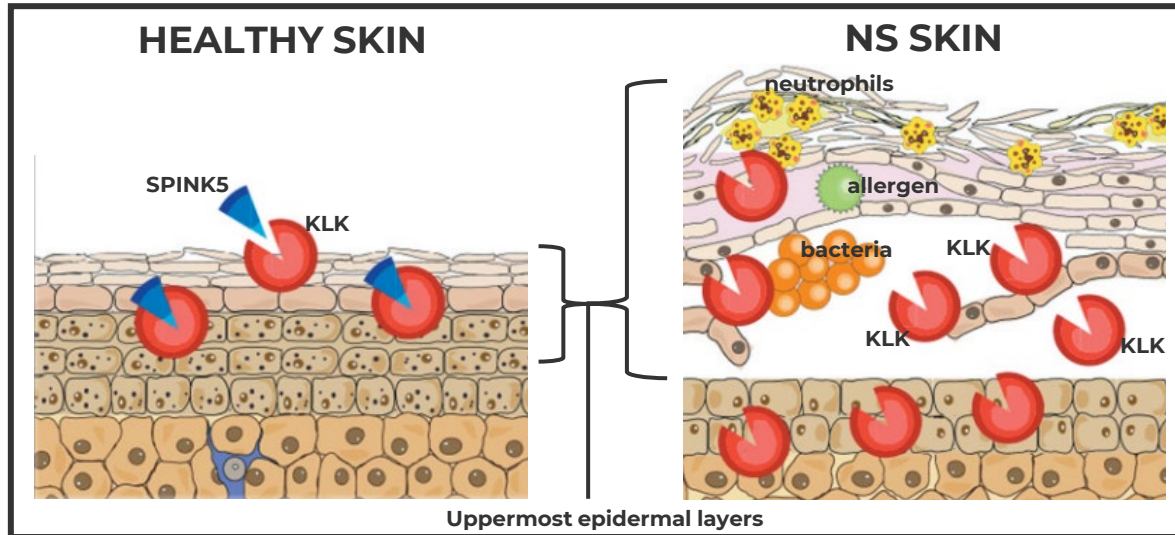


Next milestone: initial data in 2025

1. Based on healthcare claims analysis

Image: <https://www.nethertonsyndrome.com/about-nethertons.php>

BCX17725 addresses the underlying disease biology in Netherton syndrome



Modified from Petrova and Hovnanian, 2020 *Expert Opinion Orphan Drugs*

- Patients with NS have a mutation in the SPINK5 gene which causes a deficiency in the SPINK5 protein
- The SPINK5 protein is an important natural regulator of KLK5, a serine protease involved in skin turnover
- Unregulated KLK5 activity causes symptoms of NS by preventing formation of healthy skin barrier
- BCX17725 targets KLK5, providing functional replacement of the missing regulator protein to correct disease biology
- BCX17725 has the potential to improve both dermatologic and atopic disease symptoms

Addressing DME with a potent plasma kallikrein inhibitor: avoralstat suprachoroidal injection¹

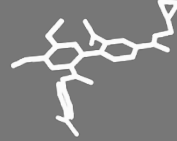
Alternative
MOA



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



Avoralstat has ideal properties for ophthalmic dosing: high potency and low solubility/depot effect

Potential for disease modifying outcomes + extended dosing interval

Significant
market
opportunity



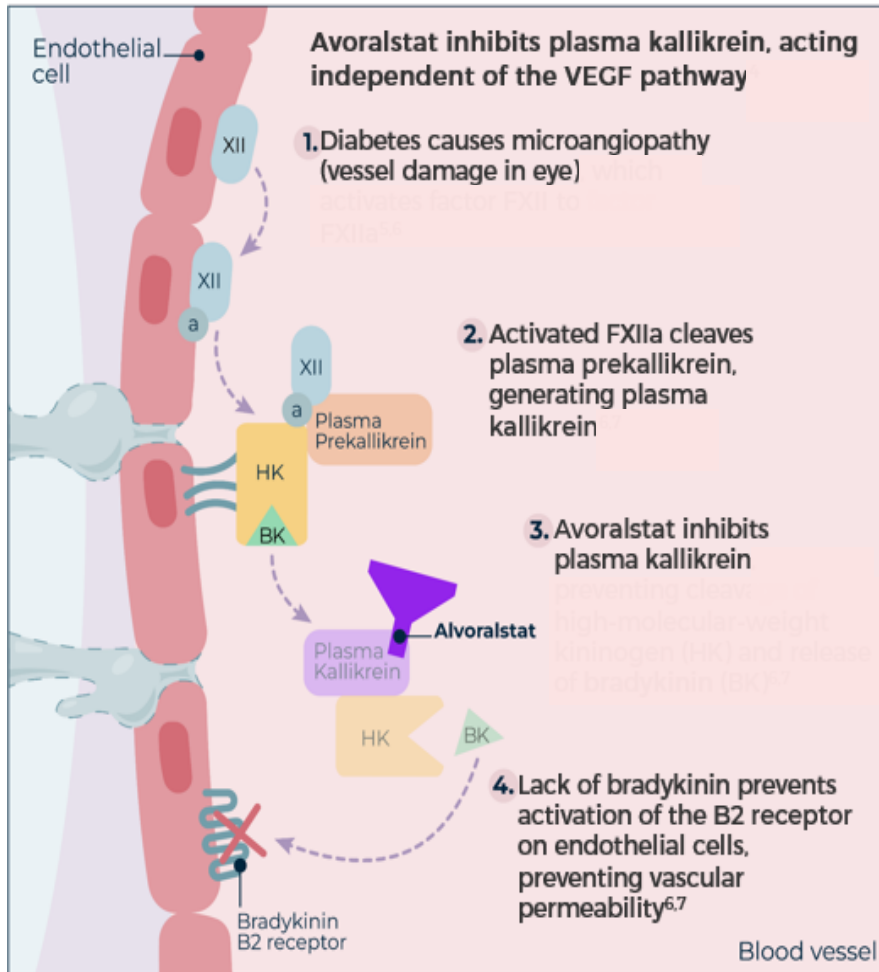
~1.5M DME patients in US

Est. \$4B VEGF market by 2028

Next milestone: begin patient studies in 2025

Avoralstat: a potent drug targeting DME

Potential to treat all DME Patients via VEGF-independent pathway



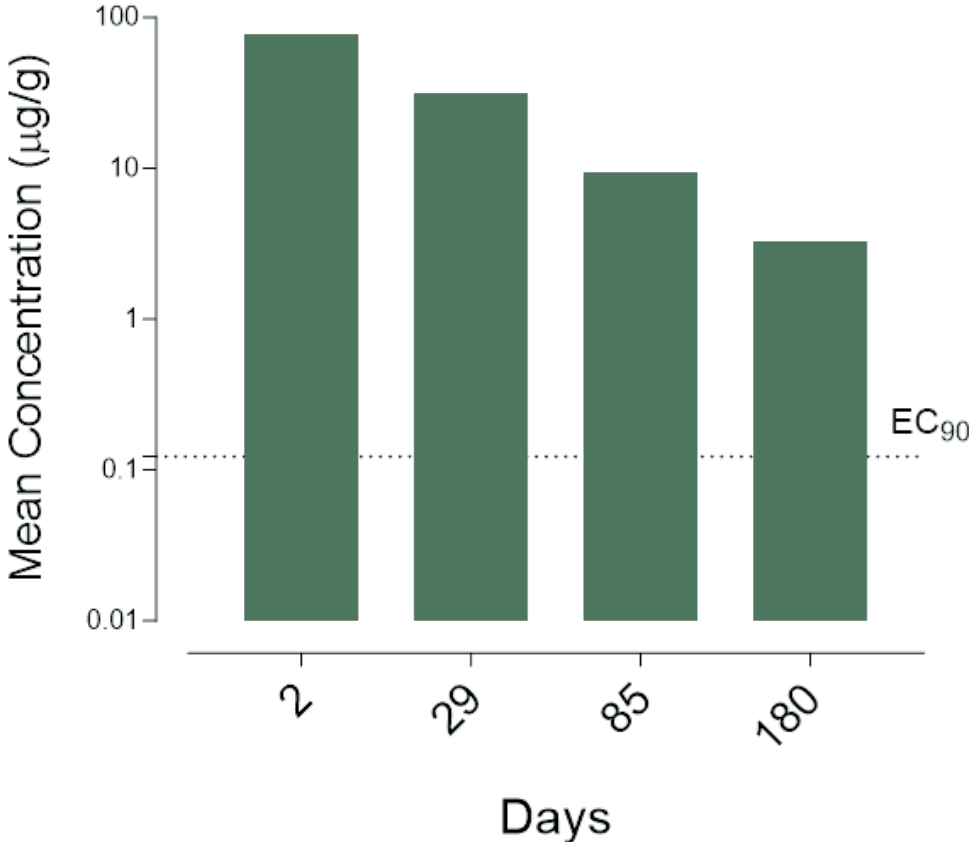
- Hyperglycemia damages retinal vasculature
- Damaged endothelium activates plasma Kallikrein (pKal)
- Elevated pKal levels seen in vitreous of DME patients
- Elevated pKal produces bradykinin leading to vascular leakage
- Avoralstat blocks pKal and bradykinin production
- Avoralstat has similar effect to VEGF inhibitors in well-established non-clinical model

BK, bradykinin; HK, high molecular weight kininogen

1. Trinh HM, et al. *World J Pharmacol.* 2016;5(1):1-14. 2. Yang S, et al. *Front. Pharmacol.* 2021;12:727870. 3. Kita T, et al. *Diabetes.* 2015;64(10):3588-3599. 4. Lang GE, et al. *TSVT.* 2020;9(4):1-12.

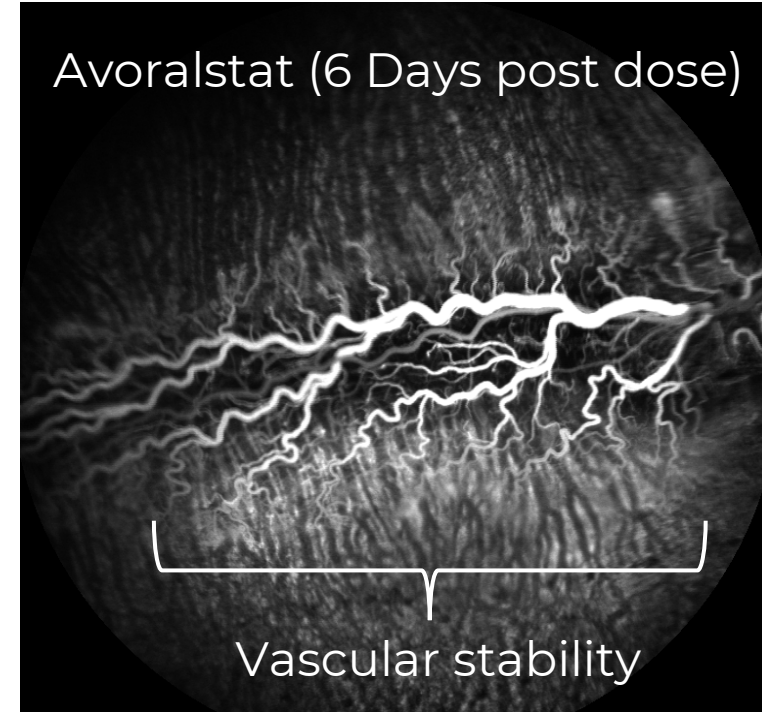
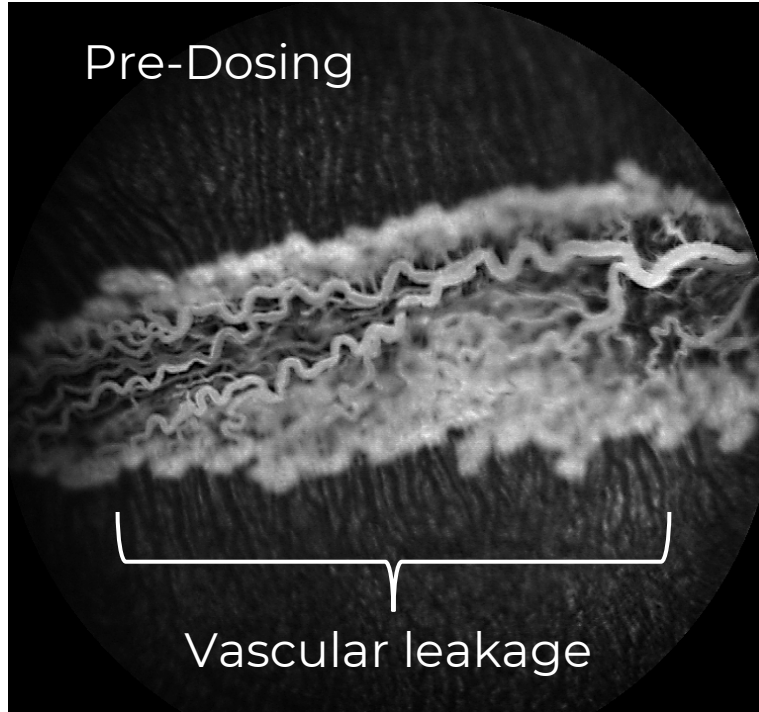
Suprachoroidal depot leads to 3+ months of sustained avoralstat levels in the retina¹

Avoralstat Retina Levels in Rabbits
Dose: 2 mg/eye



1. BioCryst Pharmaceuticals nonclinical data on file 2025

Avoralstat has similar effect to VEGF inhibitors in well-established nonclinical model¹



Financial independence and clear path to profitability

2024

Full year
operating profit¹



2025

Approach quarterly
positive EPS & cash-
flow in 2H

2026

Full year
positive EPS &
cash-flow

1. Excluding stock-based compensation expense

Key milestones in 2025

2025

File pediatric NDA for ORLADEYO

2025

Begin avoralstat clinical evaluation in patients

2H25

Obtain initial BCX17725 clinical data

2H25

Approach sustainable quarterly positive EPS & cash flow

Finance summary

(Figures in millions)

Q3 2024 CASH POSITION

Cash, cash equivalents, restricted cash & investments at December 31, 2023	\$391
Cash, cash equivalents, restricted cash & investments at June 30, 2024	\$338
Cash, cash equivalents, restricted cash & investments at September 30, 2024	\$352
Senior credit facility ^A	\$324

2025 FY GUIDANCE

ORLADEYO revenue	\$515-535
Total product revenue	\$540-560
Operating expenses	\$485-495
Operating expenses (excluding stock-based compensation)	\$425-435

A – From Pharmakon Advisors, \$300M drawn at issuance in Q2 2023. The \$324M balance above represents \$300M initial issuance plus PIK interest to-date (did not elect the PIK option for Q3 2024; the PIK option has now expired)

Traditional debt and royalty breakdown

	September 30, 2024	December 31, 2023
Royalty financing obligations - current	33,000	23,565
Royalty financing obligations - long-term	481,775	508,034
Total royalty financing obligations	514,775	531,599
Secured term loan	314,333	303,231

	Traditional Debt	Commercial Royalty
Initial amount	\$300M term loan	\$425M royalty upfronts
Partner(s)	Pharmakon (2023)	RP (2020, 2021) ^A OMERS (2021) ^A
Description	<ul style="list-style-type: none"> 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 	<ul style="list-style-type: none"> 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

A – Royalty terms described on next slide

Royalty obligations: terms

	Upfront	Product	Rate Tiers (Key Territories ^B)	Rate Tiers (Other Markets ^B)	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 ^A	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

A – Royalty Pharma made an additional \$50M equity investment in conjunction with the 2021 Royalty Purchase Agreement

B – The “Key Territories” include the United States, key European markets and other markets where ORLADEYO is sold directly or through distributors. The “Other Markets” include revenue from licensees outside the Key Territories.