

Fourth Quarter 2024 Results Call

Corporate Update & Financial Results

February 24, 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

Anthony Doyle
Chief Financial Officer

Q&A

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



2024 highlights and 2025 outlook

COMMERCIAL EXCELLENCE

- 2024 Results: \$438M global ORLADEYO revenue (34% growth) and \$451M total revenue
- Over 1,200 US prescribers
- Commercially available in over 30 countries

CLINICAL PROGRESS

- ORLADEYO pediatric program on track for NDA submission to FDA in 2025
- BCXT7725 (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 non-GAAP operating expense¹

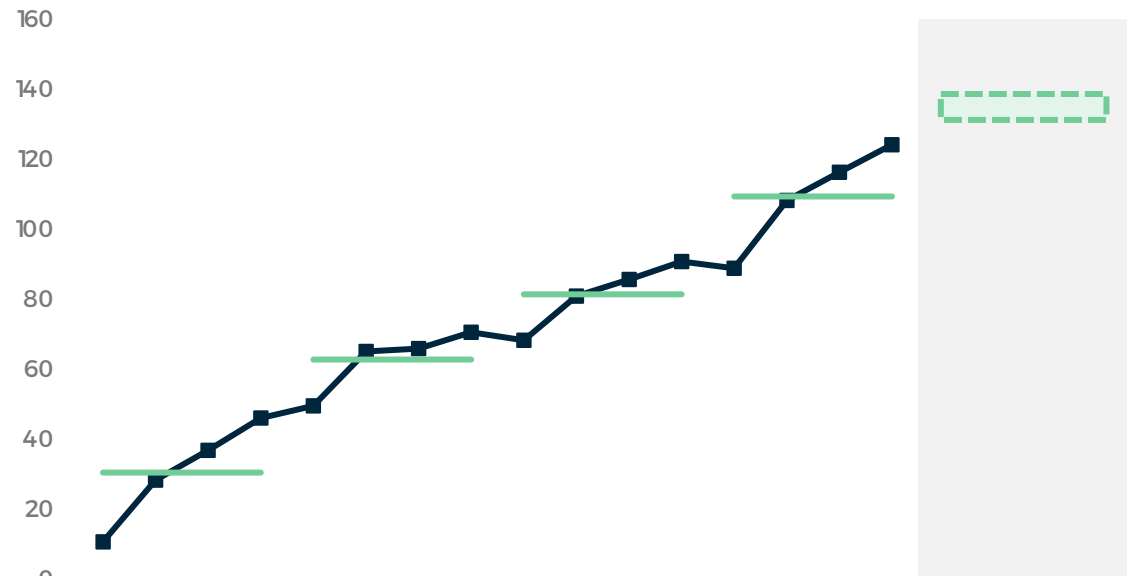
2025 GUIDANCE

- ORLADEYO: \$535-550M (previously \$515-535M)
- Total revenue: \$560-575M (previously \$540-560M)
- Non-GAAP operating expense¹: \$425-435M

¹ Not including stock-based compensation

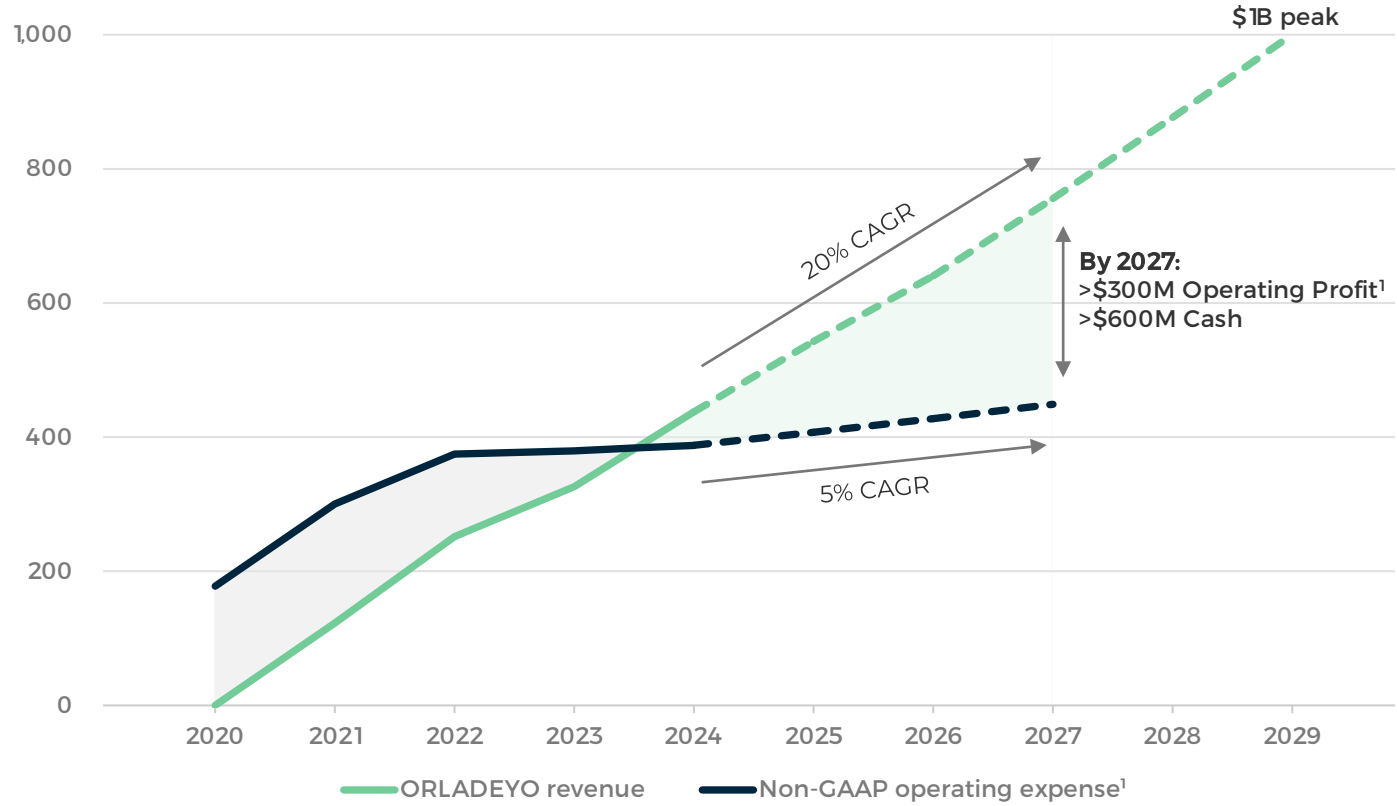
Strong ORLADEYO growth to continue in 2025

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)	123				252				326				438				535-550			
Growth (\$M)	+123				+129				+74				+112				+97-112			
Growth (%)	-				+105%				+29%				+34%				+22-26%			

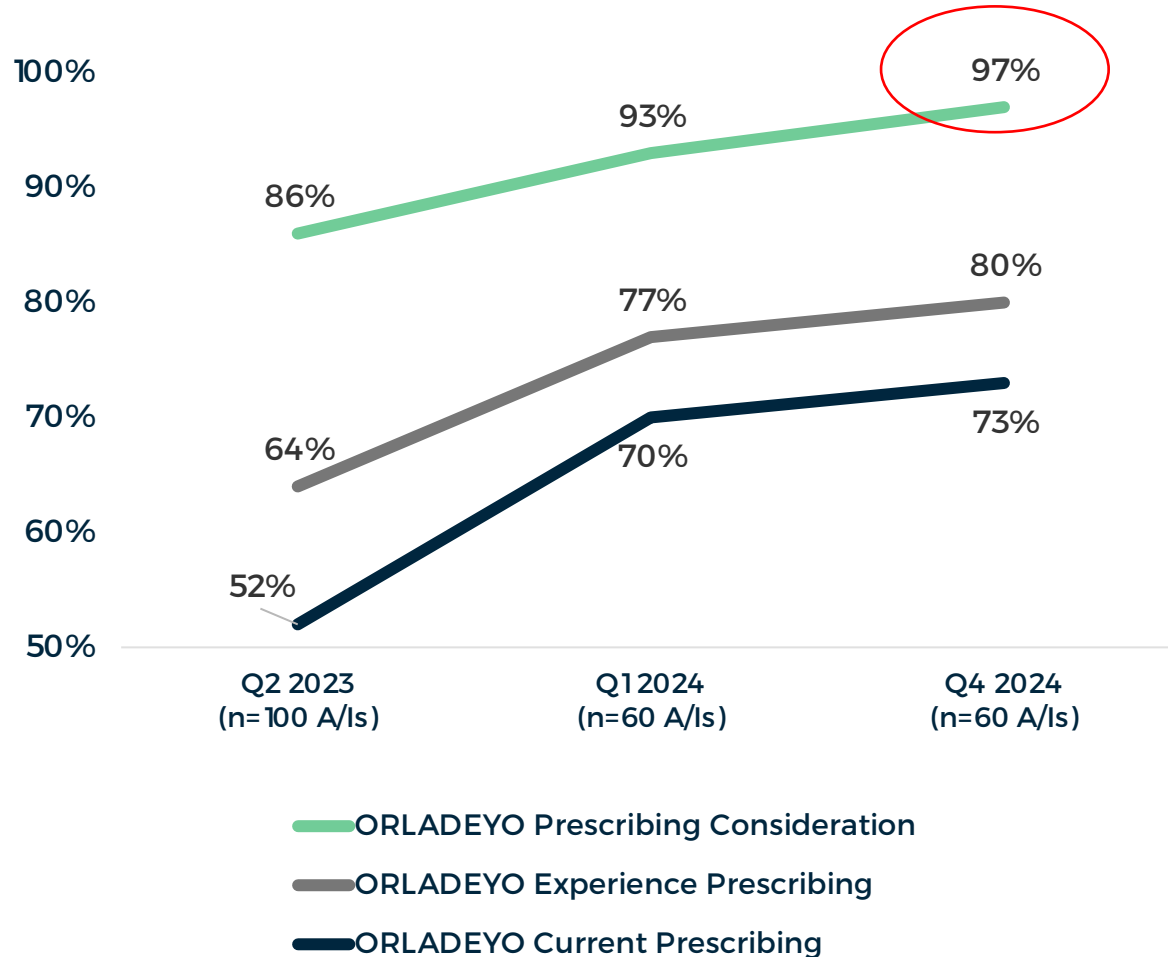
ORLADEYO growth + focused capital allocation to drive sustained profitability



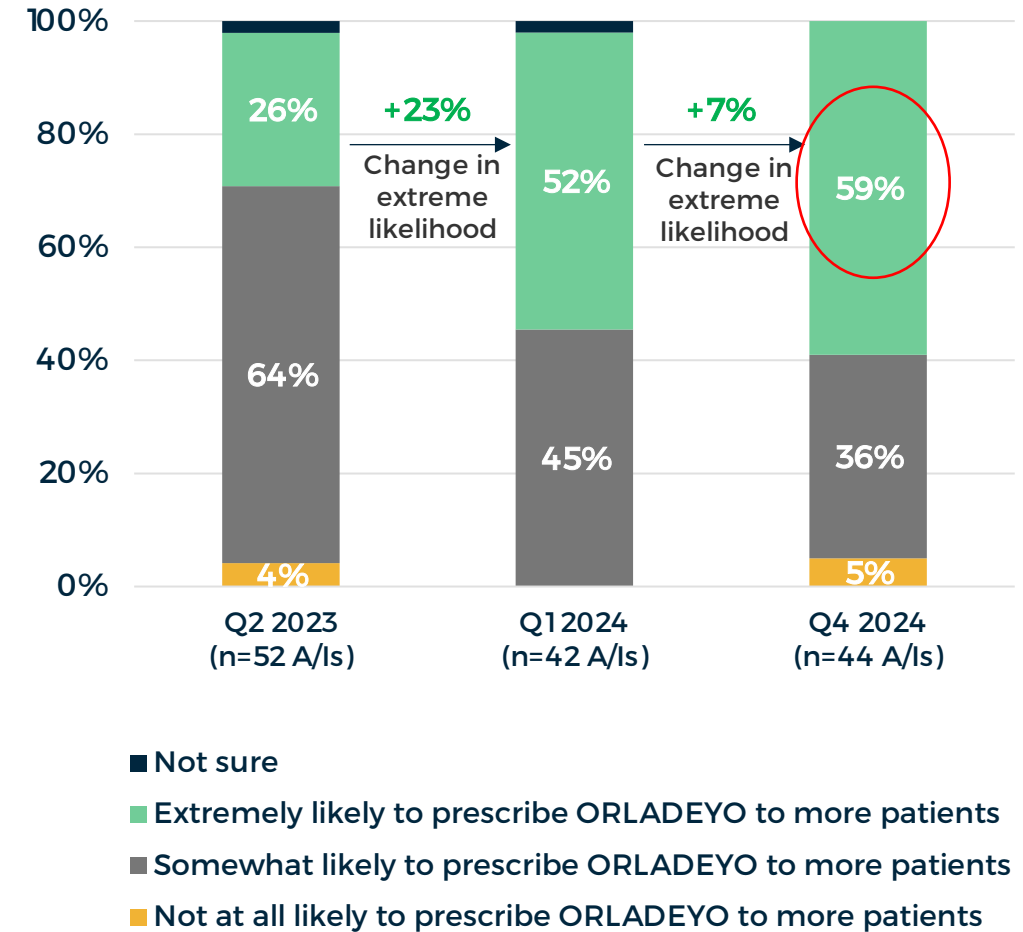
1. Not including stock-based compensation

MARKET RESEARCH: Allergist/Immunologist prescribing has grown significantly while current prescribers still intend to prescribe more

ORLADEYO PRESCRIBING METRICS



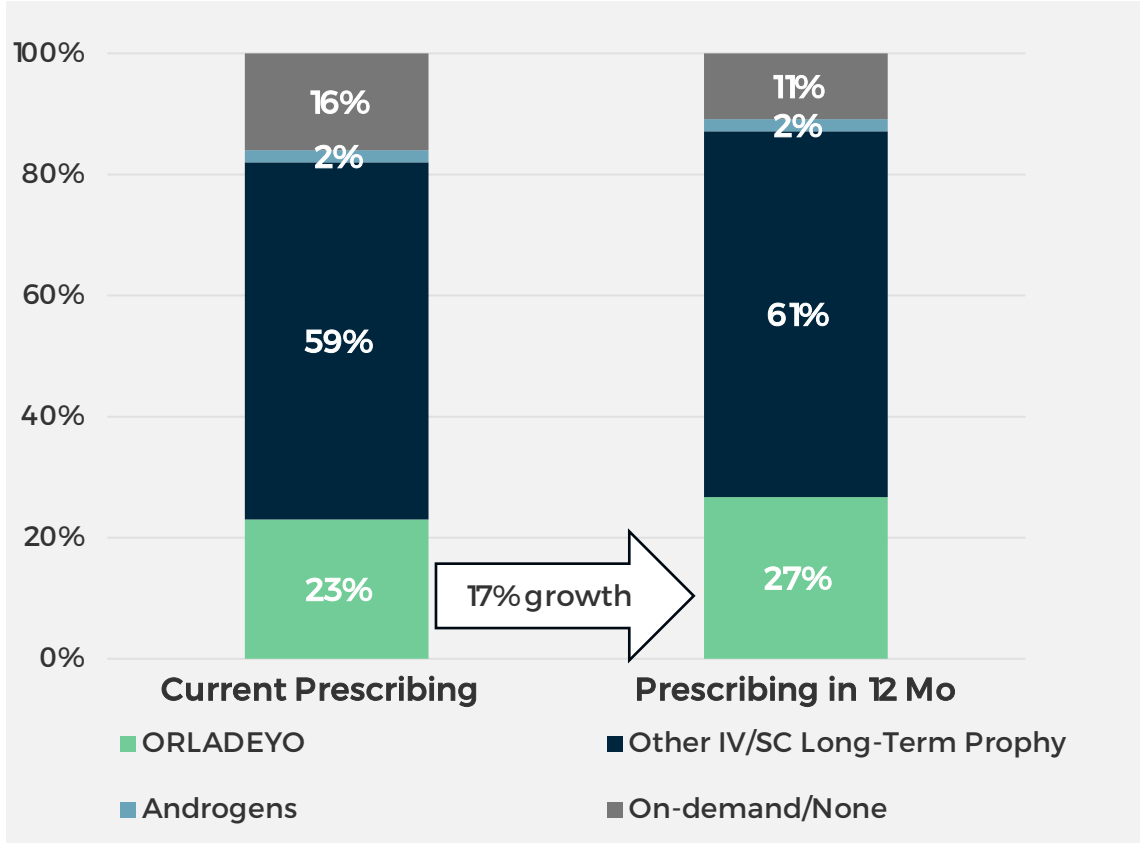
LIKELIHOOD TO PRESCRIBE ORLADEYO TO MORE PATIENTS



Source: BioCryst Internal Market Research Studies (Conducted Dec 2023, Feb 2024, Dec 2024)

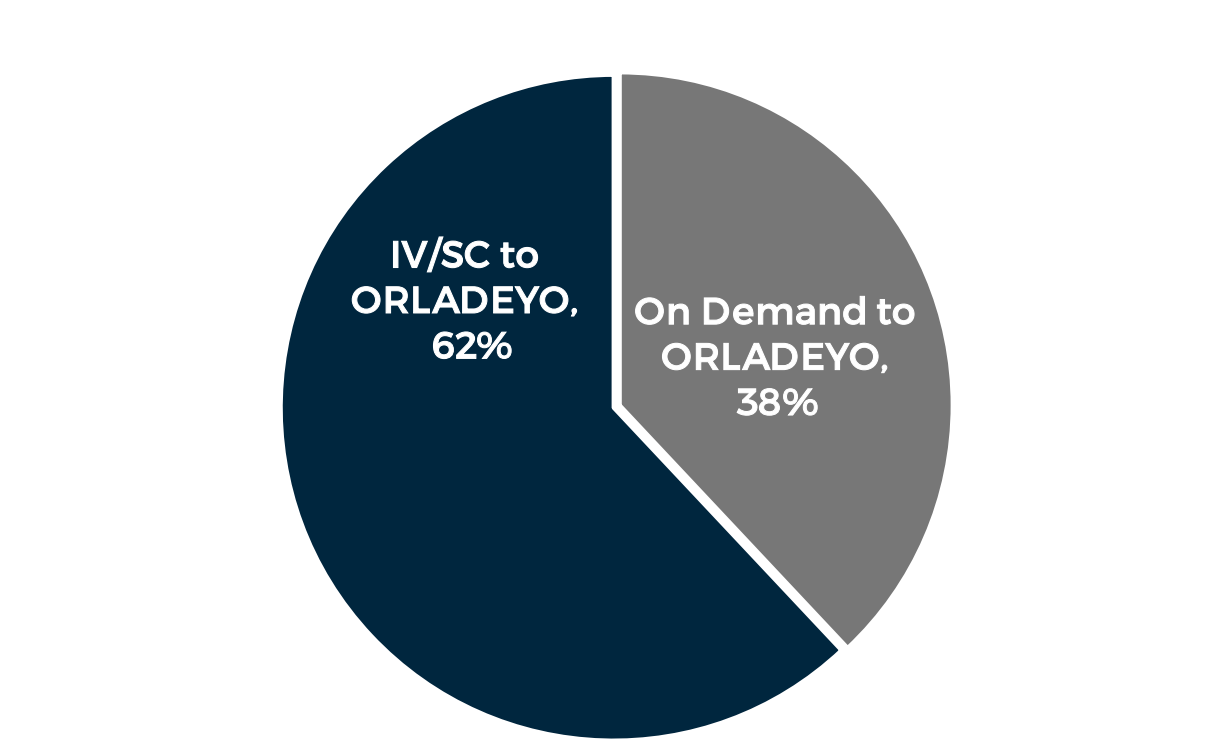
MARKET RESEARCH: Intent to prescribe more ORLADEYO remains consistent, with prescriptions coming mostly from prophylactic switches

ALLERGIST-IMMUNOLOGISTS (A/Is) PRESCRIBING – Q4 '24
(n=60 unique A/Is managing 660 HAE patients)



Future ORLADEYO prescribing has been consistent throughout all of 2023-24

SOURCE OF FUTURE NEW ORLADEYO PRESCRIPTIONS – Q4 '24
(n=60 unique A/Is managing 660 HAE patients)

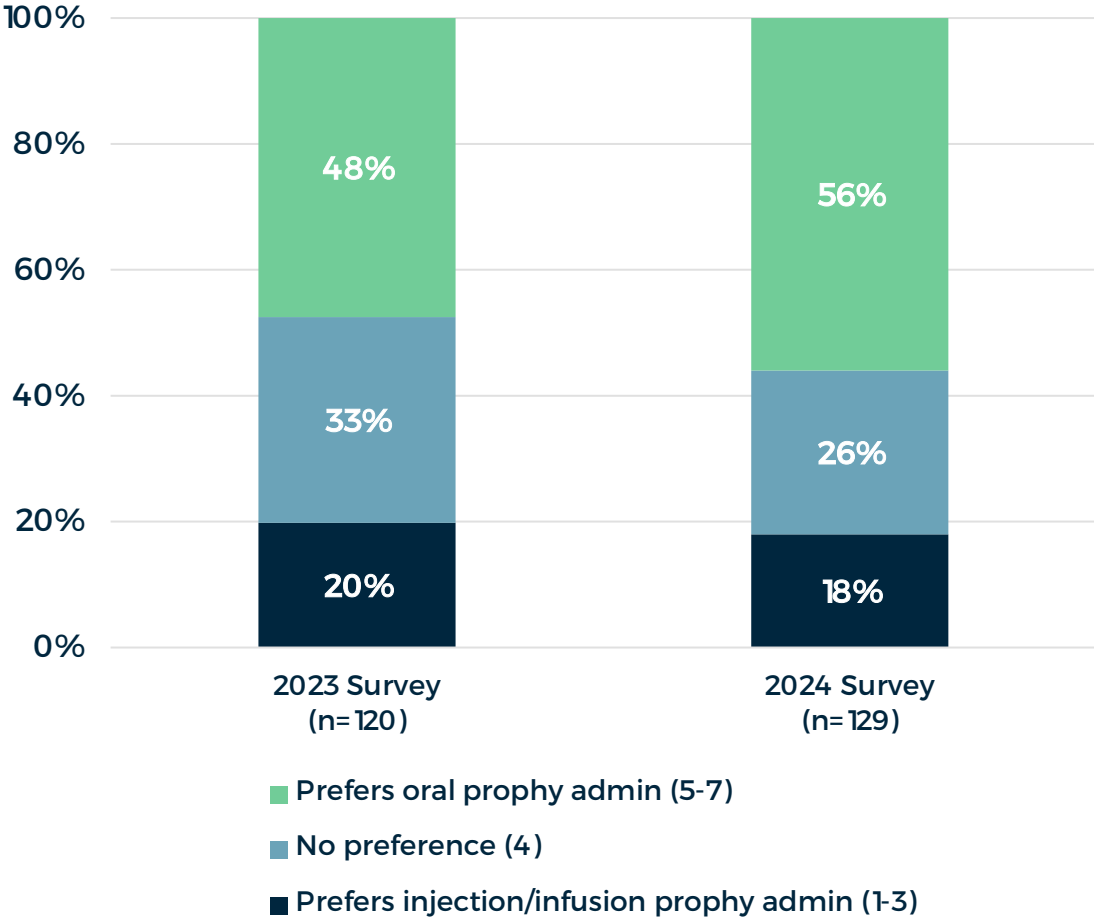


A/Is expect future new ORLADEYO prescriptions to come ~2/3 from prophylaxis switches and ~1/3 from On-Demand Only

Source: BioCryst Internal Market Research Studies (Conducted Dec 2024)

MARKET RESEARCH: Patients on injectable LTP consistently show strong preference for oral route of administration

ROUTE OF ADMIN PREFERENCE AMONG CURRENT INJECTABLE PROPHY USERS
Current Injectable Users (n=249)



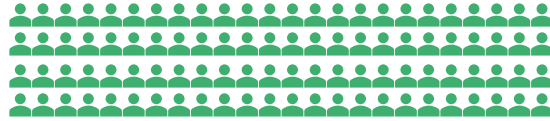
Source: BioCryst Internal Market Research Studies (Conducted Oct 2023, Jan-Feb 2023, Jan-Feb 2024)

Comprehensive annual research + market simulation

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

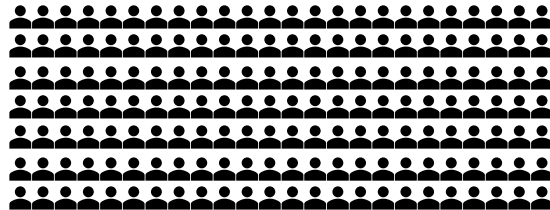
Research Sample*

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

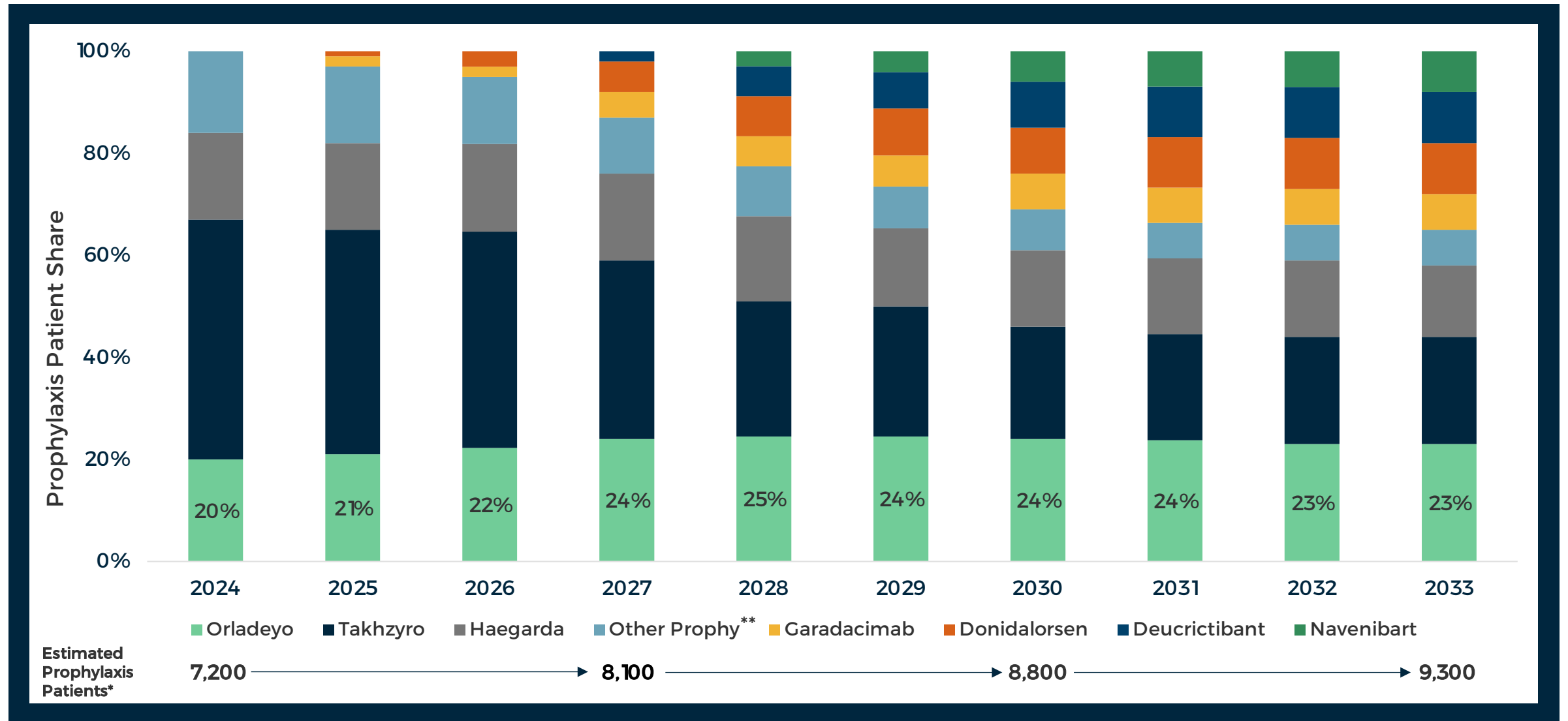
1	Single Interaction & Decision	
3	Single Simulation Run	<p><i>Prophy</i></p> <p><i>Acute Only</i></p> <p><i>No HAE Med</i></p> <p><i>New Patient</i></p>
4	Full Market Simulation Approach	

* Choice-based conjoint

** HAE treaters: Allergists & Immunologists

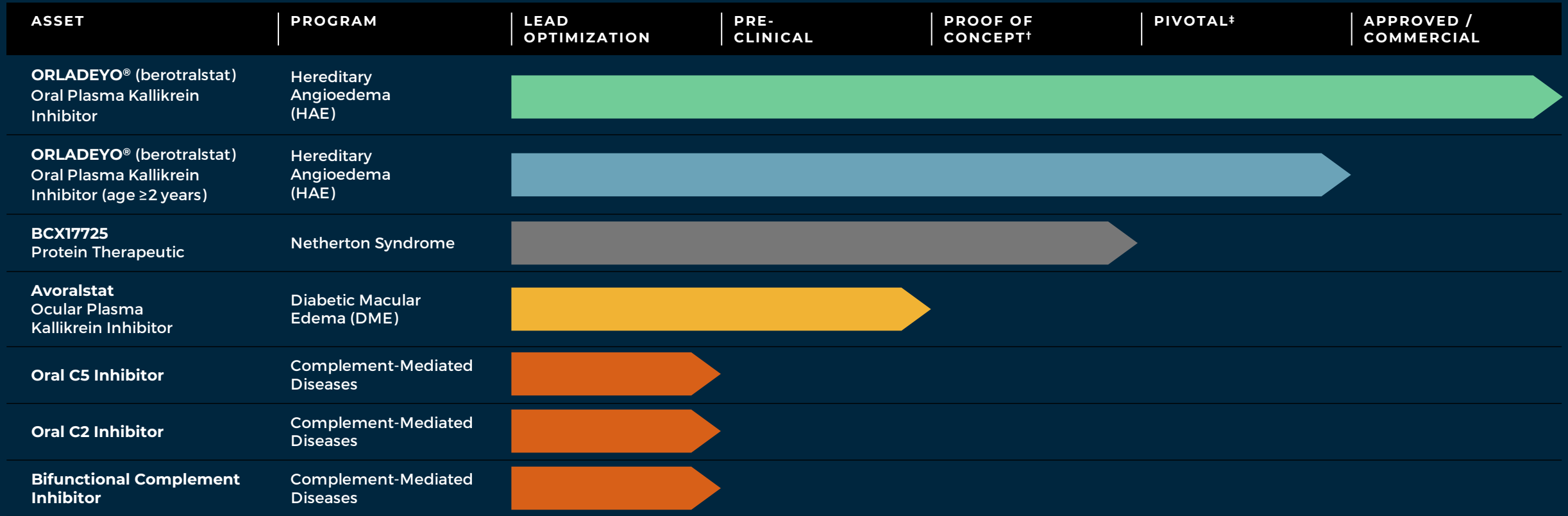
Monte Carlo simulation outcome: U.S. prophylaxis market share

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 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

On track for NDA filing in 2025

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

High
unmet
need



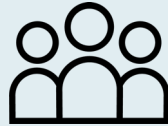
Severe, rare, genetic and lifelong disease with no approved targeted therapies

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
treatment²



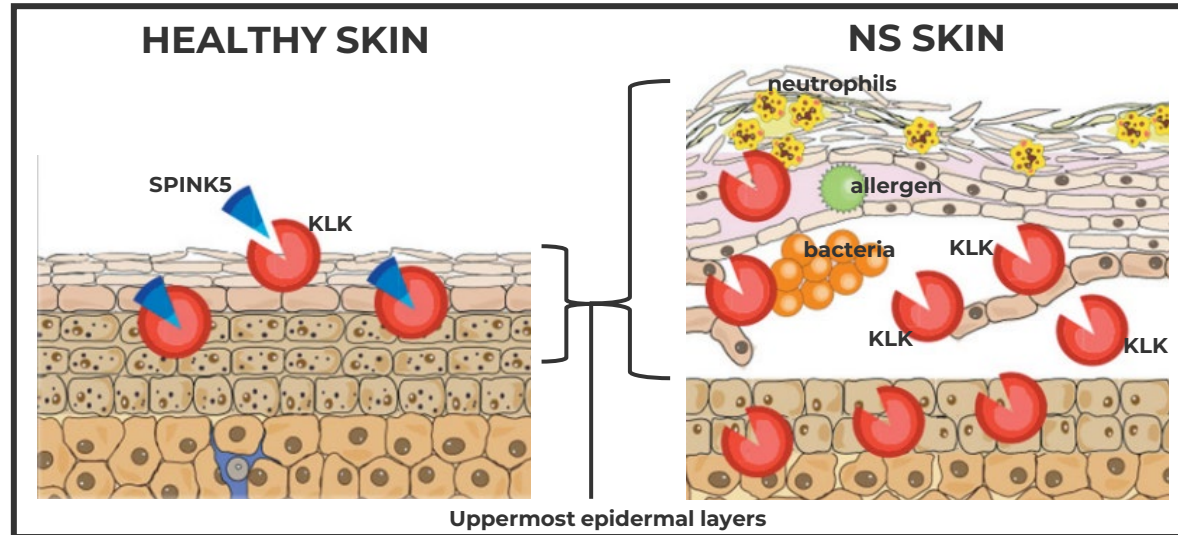
Next milestone: initial data in 2025

1. Based on healthcare claims analysis.

2. Based on precedent from HAE and ultra-rare diseases.

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*¹

- 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

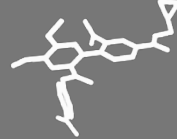
Alternative
MOA



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



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

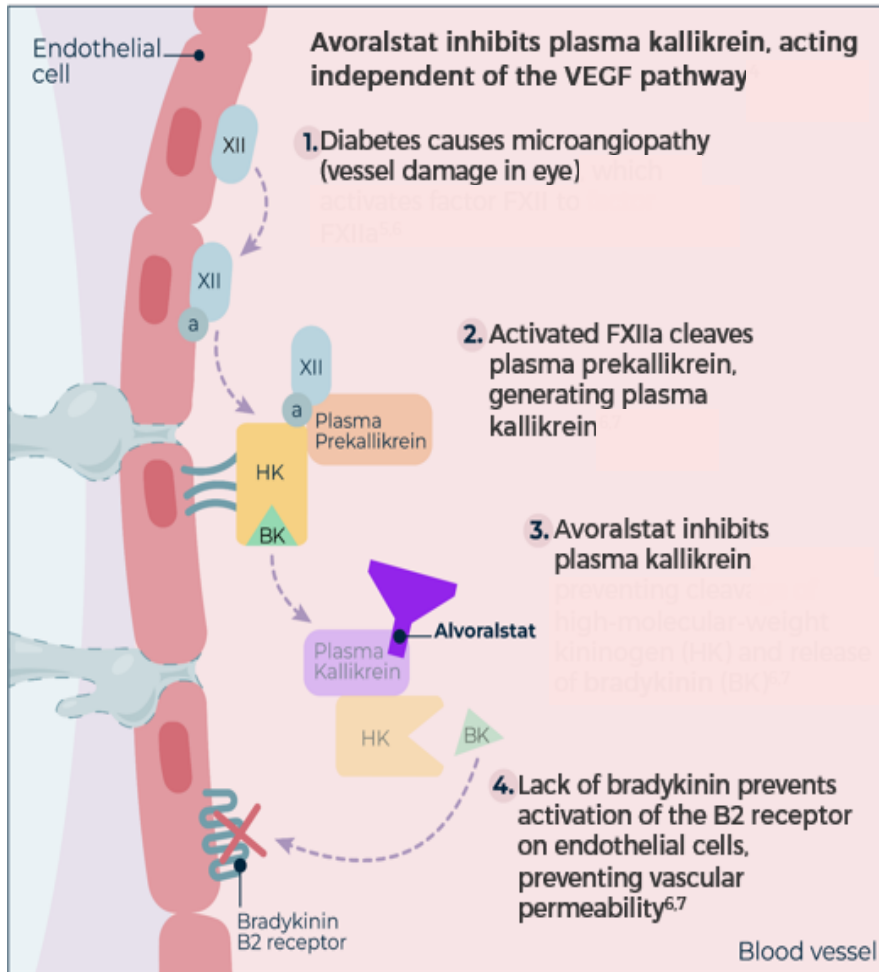
Est. \$4B VEGF market by 2028

Next milestone: begin patient studies in 2025

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

Avoralstat: a potent drug targeting DME

Potential to treat all DME Patients via VEGF-independent pathway

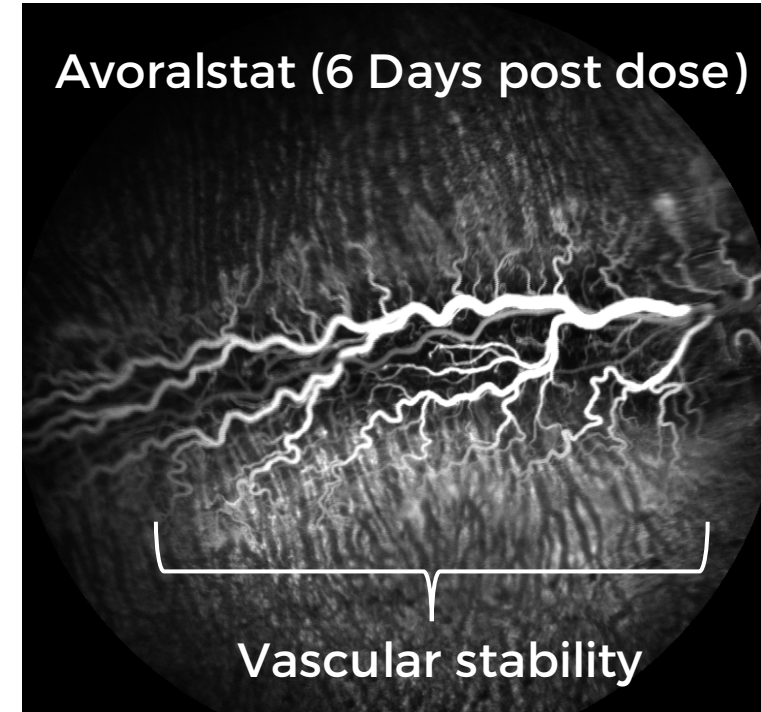
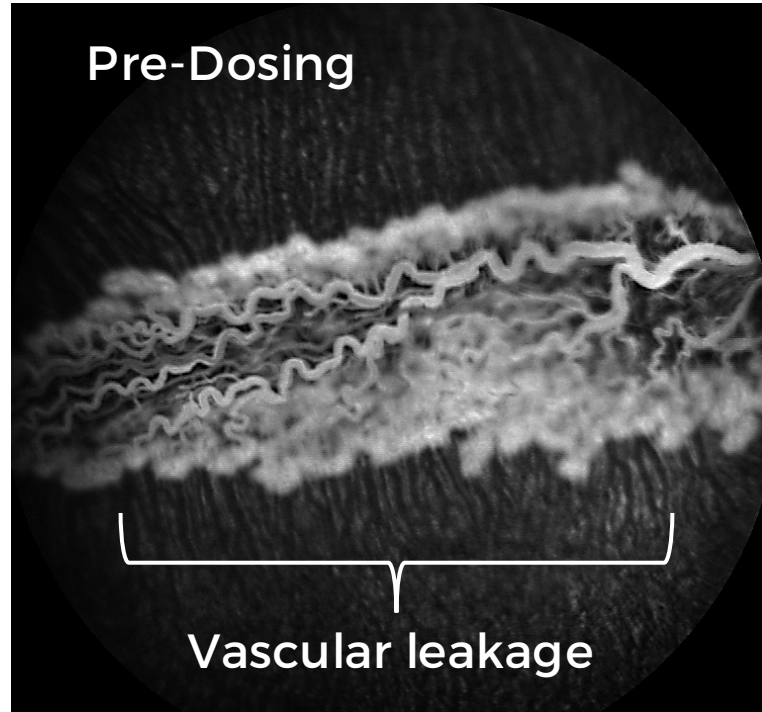


- Hyperglycemia damages retinal vasculature
- Damaged endothelium activates plasma Kallikrein (pKal)
- Elevated pKal levels seen in vitreous of DME patients
- Elevated pKal produces bradykinin leading to vascular leakage
- Avoralstat blocks pKal and bradykinin production
- Avoralstat reduces retinal vascular leakage in 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.

Preclinical evidence demonstrates plasma kallikrein pathway may reduce vascular leakage

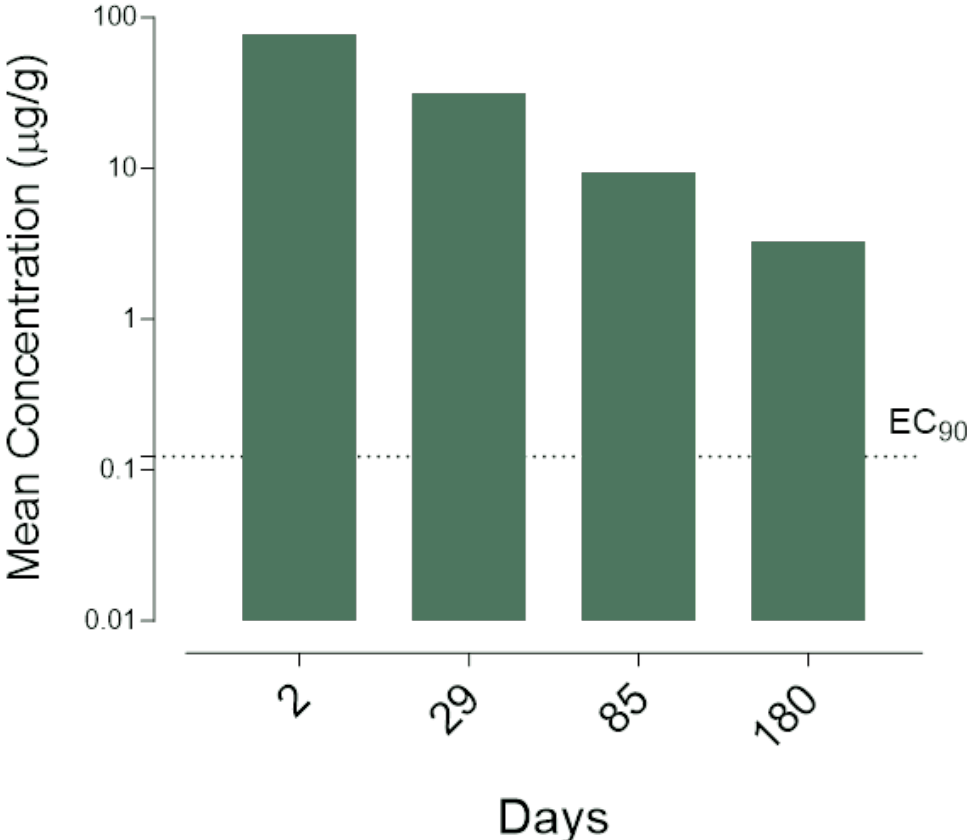


Source: BioCryst Pharmaceuticals nonclinical data on file 2025., Kumar et al. Int J Ophthalmol. 2022 Jan 18;15(1):15-22

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 retina¹

Avoralstat Retina Levels in Rabbits
Dose: 2 mg/eye



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.

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 Not including stock-based compensation

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)

Q4 2024 CASH POSITION

Cash, cash equivalents, restricted cash & investments at December 31, 2023	\$391
Cash, cash equivalents, restricted cash & investments at December 31, 2024	\$343
Senior credit facility ¹	\$324

2025 FY GUIDANCE

	Prior	Current
ORLADEYO revenue	\$515-535	\$535-550
Total product revenue	\$540-560	\$560-575
Non-GAAP operating expense (not including stock-based compensation)	\$425-435	Unchanged

1. From Pharmakon Advisors, \$300M drawn at issuance in Q2 2023. The \$324M balance above represents \$300M initial issuance plus PIK interest to-date (the PIK option has now expired).

Traditional debt and royalty breakdown

	December 31,	
	2024	2023
Royalty financing obligations - current	32,676	23,565
Royalty financing obligations - long-term	481,053	508,034
Total royalty financing obligations	513,729	531,599
Secured term loan	314,869	303,231

	Traditional Debt	Commercial Royalty
Initial amount	\$300M term loan	\$425M royalty upfronts
Partner(s)	Pharmakon (2023)	RP (2020, 2021) ¹ OMERS (2021) ¹
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

1. Royalty terms described on next slide

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	155x

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