

Second Quarter 2025 Results Call

Corporate Update & Financial Results

August 4, 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, as well as statements regarding our expected future ORLADEYO royalty rates. These statements are subject to known and unknown risks, uncertainties and other factors which may cause actual results, performance, achievements, market share or size, pipeline development outcomes, or royalty rates to be materially different from any future results, performance, achievements, market share or size, pipeline development expectations, or expected royalty rates 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 and deal-related costs. 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 or deal-related costs 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. In addition, we are unable to predict with reasonable certainty the full amount of deal-related costs as the closing of the sale of our European business is still pending and the related costs are dependent on various factors that have not yet occurred. The actual amount of stock-based compensation expense and deal-related costs 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

Financial update

Jon Stonehouse

President and Chief Executive Officer

Babar Ghias

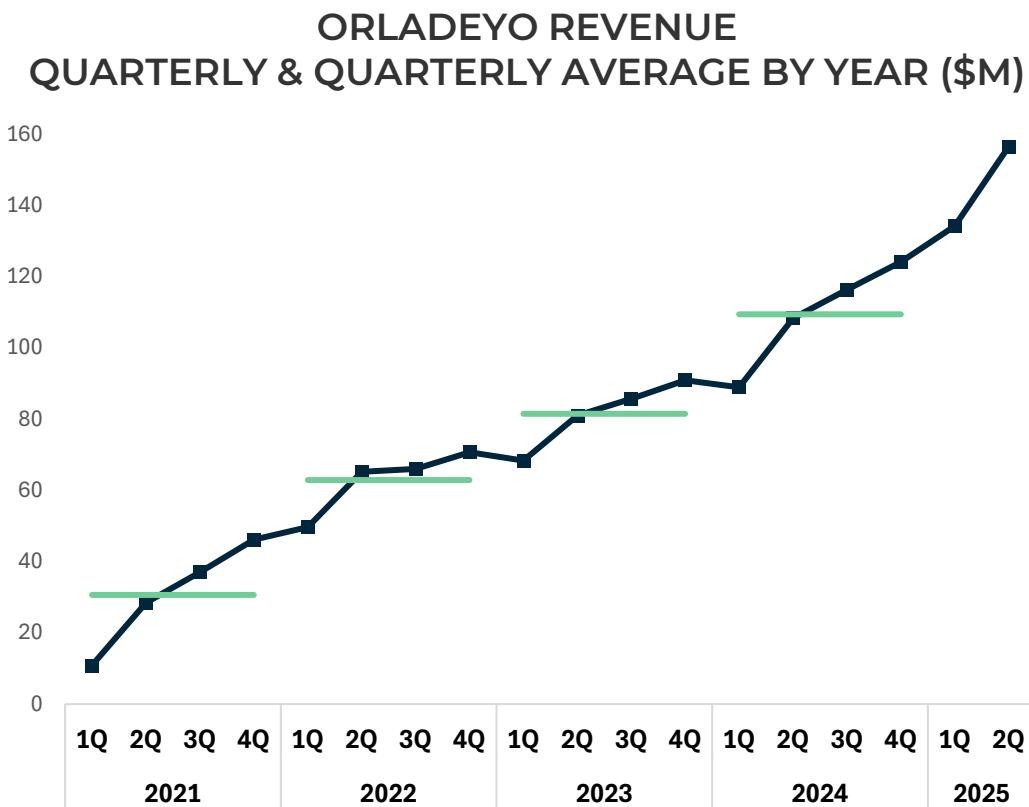
Chief Financial Officer

Q&A

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



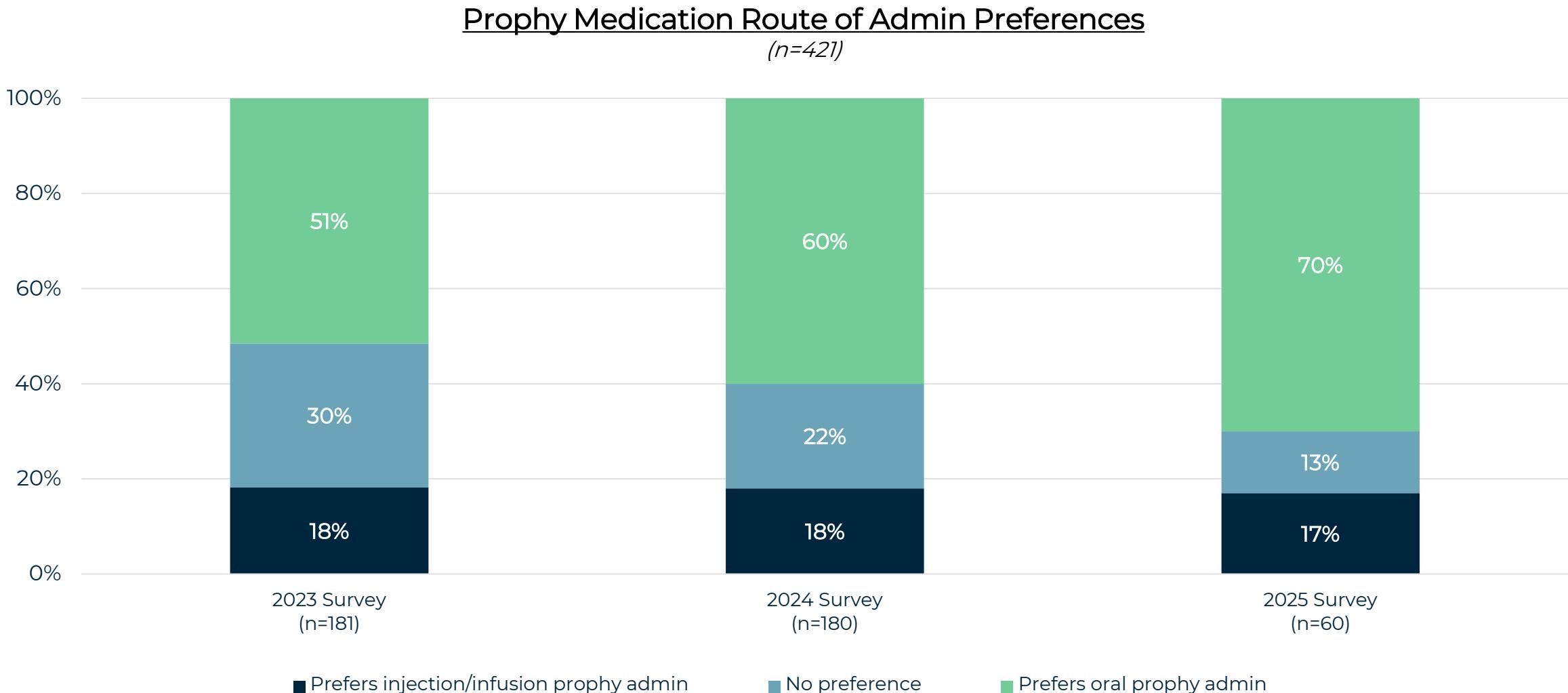
Strong Q2 led by jump in ORLADEYO demand



- Best quarter ever for new patient prescriptions in the US
- Revenue growth exceeded expectations due to:
 - Robust underlying demand (US and international)
 - Efficiency in getting paid shipments
 - Lower rate of discontinuations
 - Gross-to-net improvement
- FY25 revenue expected to meet previous guidance range (\$580-600M) even when excluding 4Q 2025 EU revenue¹

1. Sale of European ORLADEYO business to Neopharmed Gentili expected to close early in 4Q25.

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

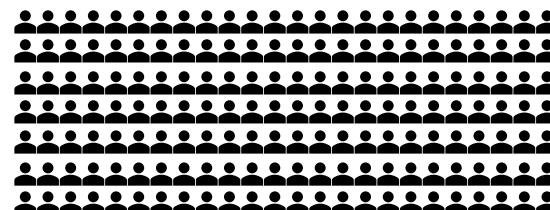
Research Sample*

PATIENTS



n=100 HAE patients

PHYSICIANS



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

PAYERS

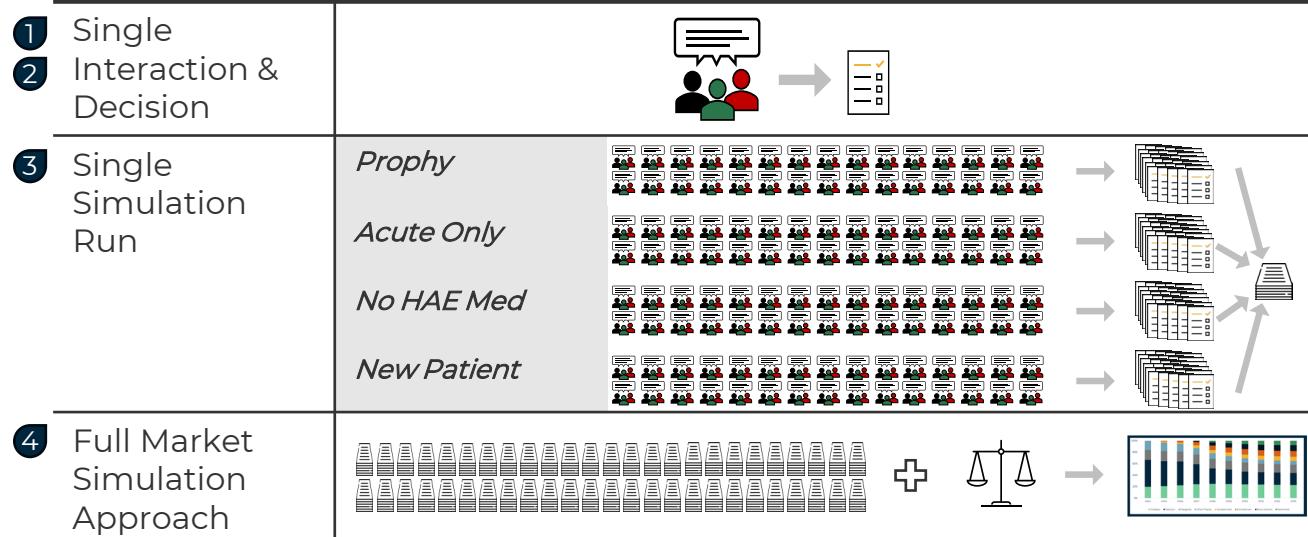


n=56 decision makers covering over 200 million total lives.

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

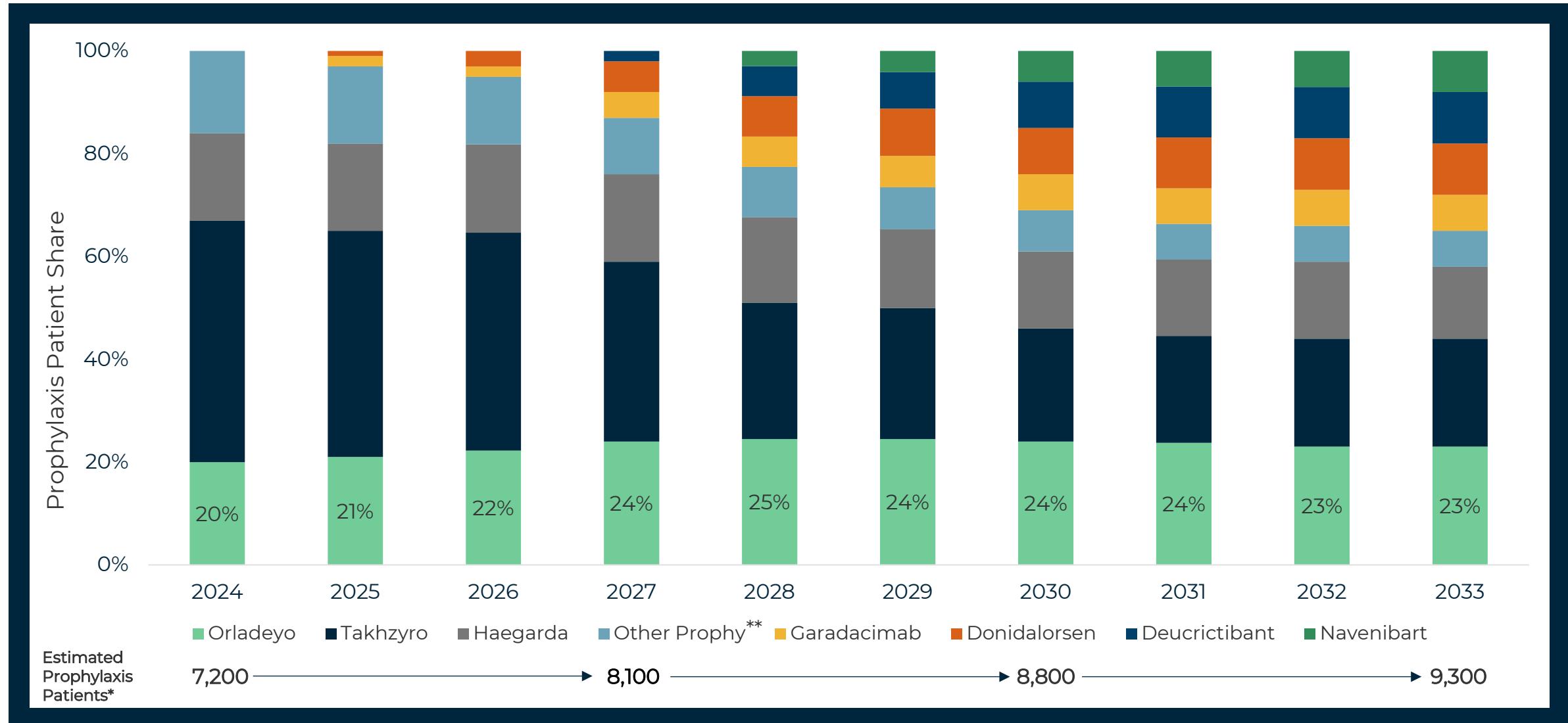


* Choice-based conjoint

** HAE treaters: Allergists & Immunologists

Monte Carlo simulation outcome: U.S. 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 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					
Avorolstat 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 avorolstat 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.

Bringing ORLADEYO granules 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

PDUFA target date Dec 12, 2025

EU & Japan applications submitted

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

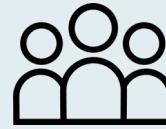
Validated target



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

BCX17725 replaces missing protein
functions

Under-diagnosed population



Diagnosed US population of ~1,600¹

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

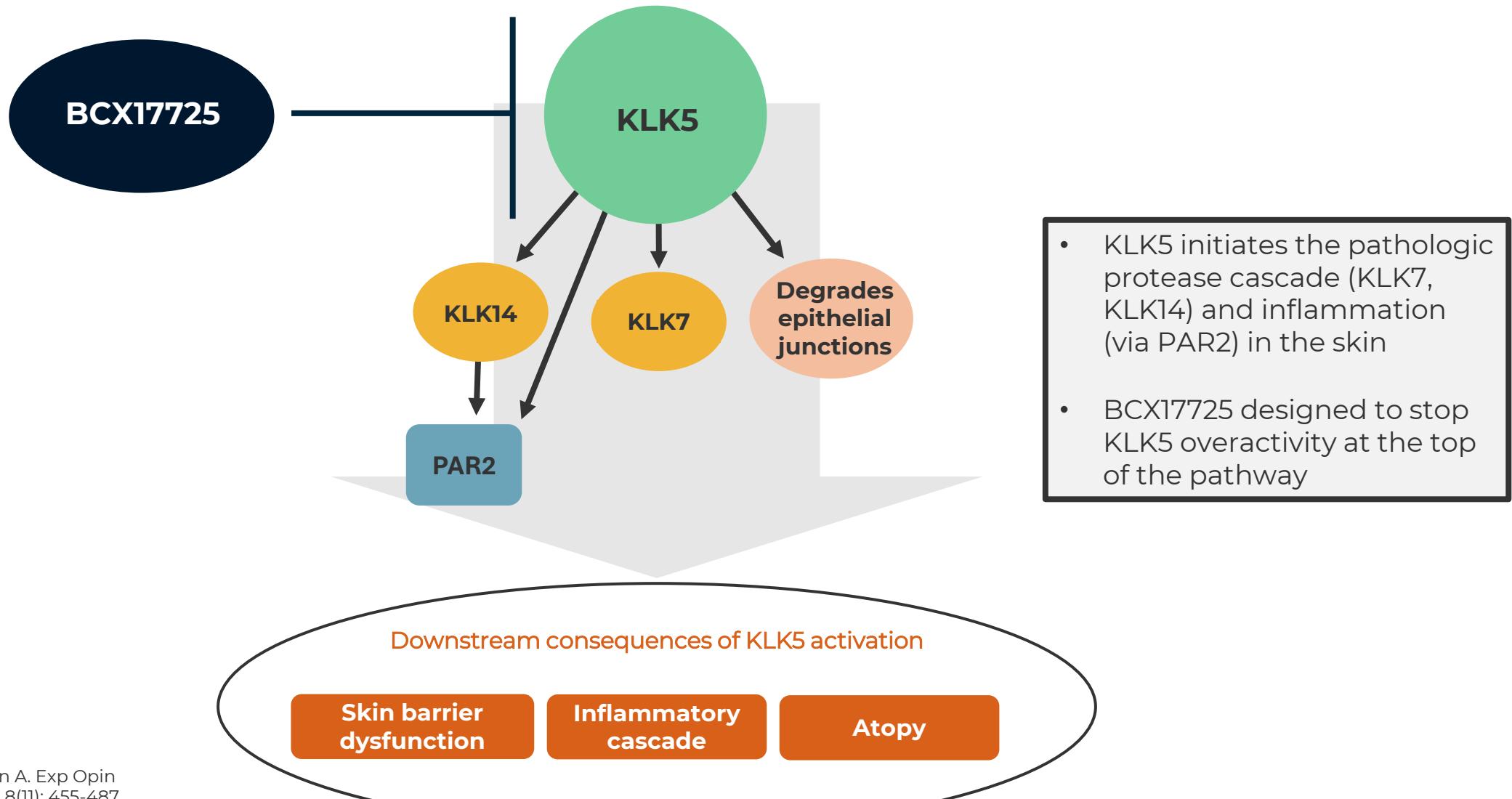


IND cleared by FDA

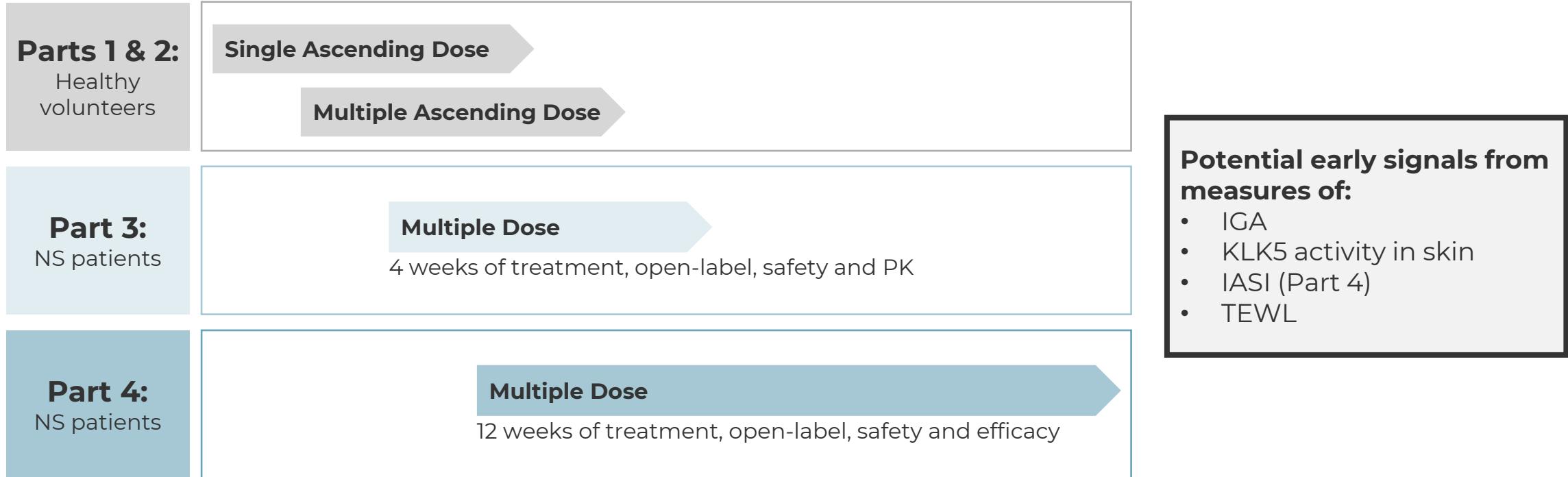
1. Based on healthcare claims analysis

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

BCX17725 targets KLK5, the key player in Netherton syndrome



BCX17725 Phase 1: healthy volunteers and patients with Netherton syndrome



IGA: Investigator's Global Assessment scale

IASI: Ichthyosis Area and Severity Index

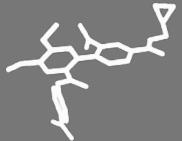
TEWL: Transepidermal Water Loss

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

Alternative
MOA



Right drug
+ delivery



Significant
market
opportunity



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

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

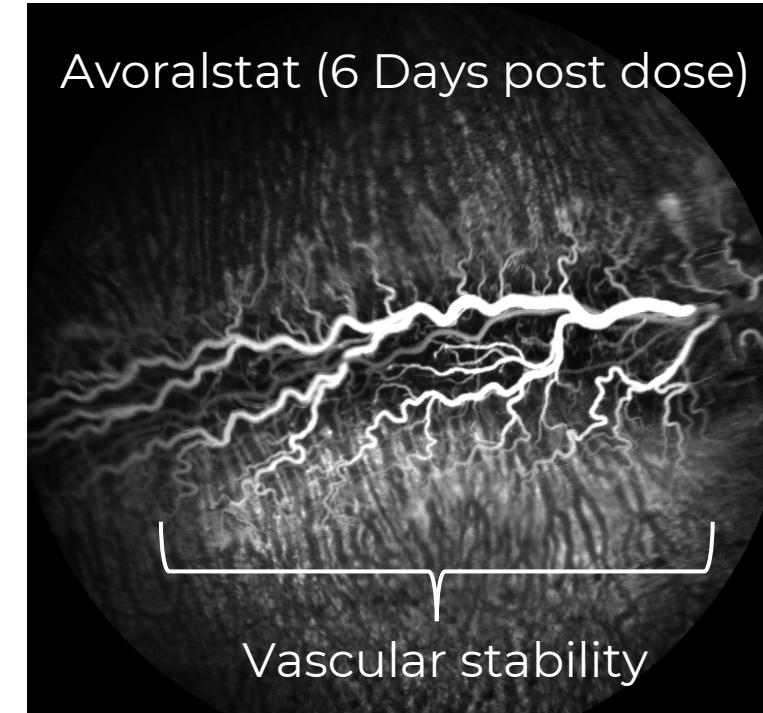
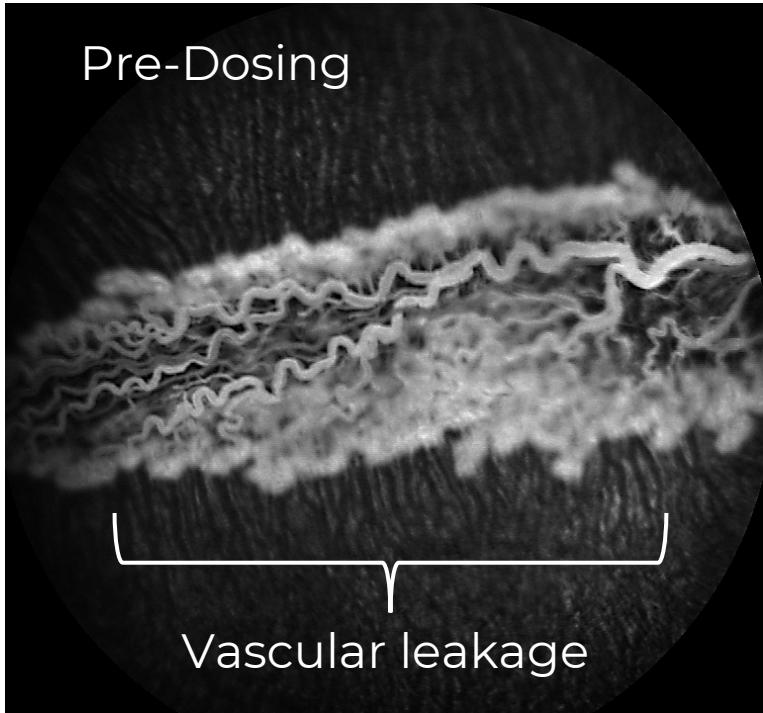
Potential for disease modifying outcomes + extended dosing interval

~1.5M DME patients in US

Est. \$4B VEGF market by 2028

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

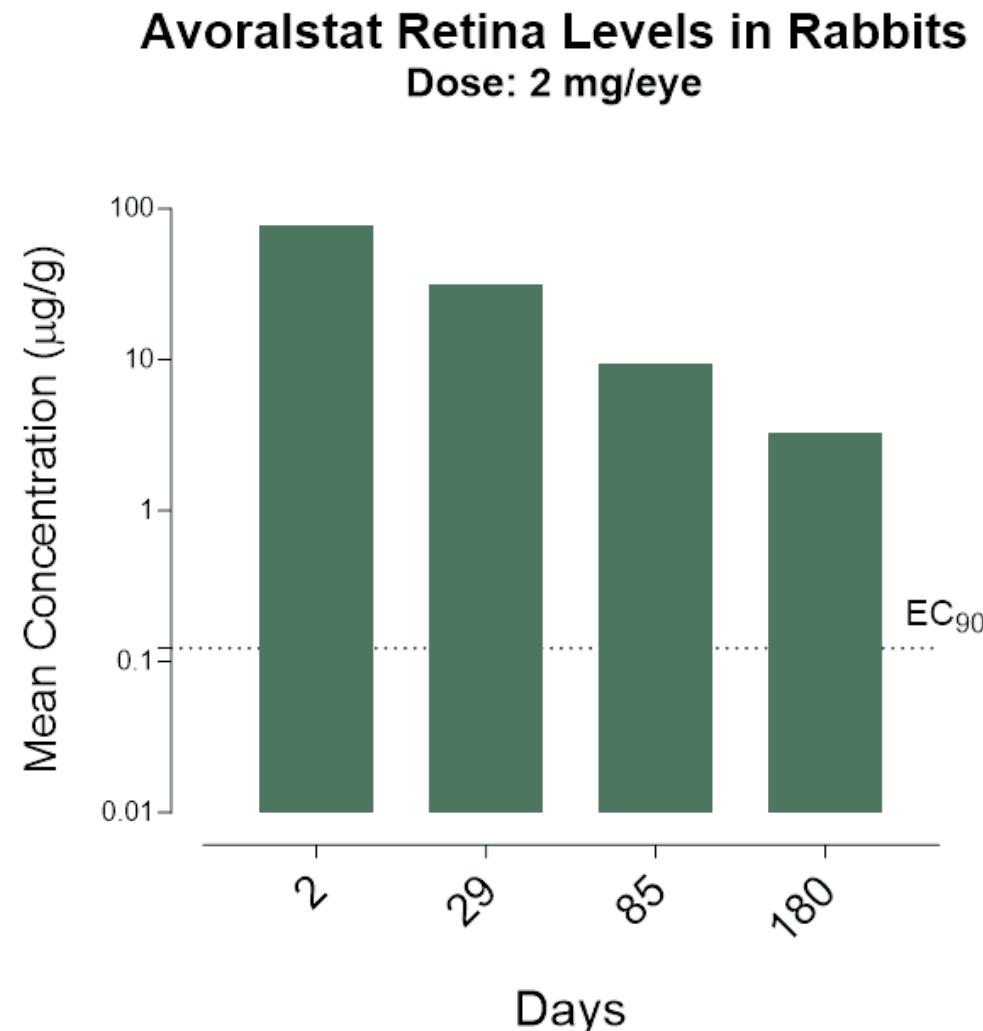
Preclinical evidence demonstrates plasma kallikrein pathway may reduce vascular leakage



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.

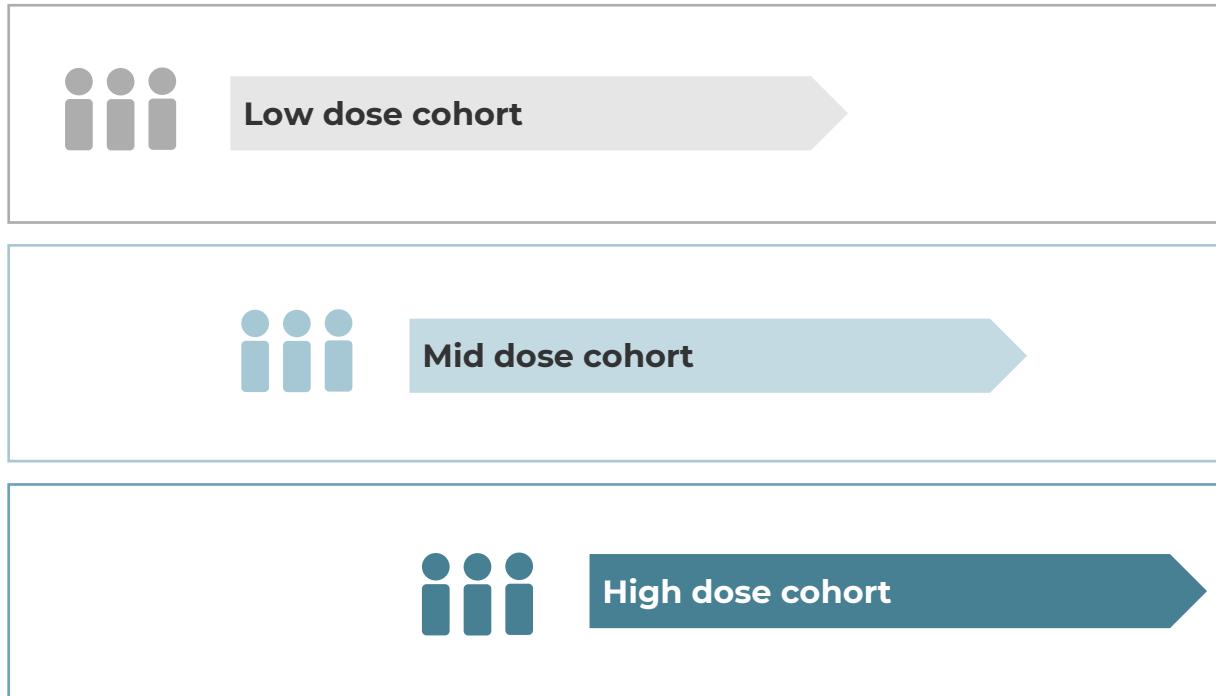
Suprachoroidal injection leads to 3+ months of sustained avorolstat levels in the retina¹



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.

Avorolstat 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

Path to profitability significantly accelerated

2024

Full year
operating profit¹

2025
2026

Achieve positive net
income & cash flows²

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 \$125 million in Pharmakon prepayments made in 2025.

Key milestones in 2025

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

Pediatric NDA for ORLADEYO

Initial BCX17725 and avorolstat clinical data

Accelerated full-year profitability and sustainable cash flow

Finance summary

(Figures in millions)

CASH POSITION	JUN 30, 2025	PRO FORMA ³	
		JUN 30, 2025	6ME
Cash, cash equivalents, restricted cash & investments ¹	\$287	\$235	
Senior credit facility	\$249	\$199	
ORLADEYO ROYALTIES	Q2 2025	JUN 30, 2025	
Royalty revenues paid and payable	\$31	\$57	
Non-cash interest expense	\$13	\$27	
Launch-to-date OMERS royalties (% progress to cap)	\$74 (32%)		
FY 2025 GUIDANCE	CURRENT	PRIOR	
ORLADEYO revenue	Unchanged	\$580-600	
Non-GAAP operating expenses ²	Unchanged	\$440-450	

1. Cash, cash equivalents, restricted cash and investments totaled \$287 million at June 30, 2025, of which \$15 million of cash and cash equivalents are held within the Company's European ORLADEYO Business and is reflected in current assets held for sale.

2. Excludes stock-based compensation and deal-related costs.

3. In July 2025, the company paid down \$50 million of the outstanding balance plus prepayment penalty and accrued interest through prepayment date.

ORLADEYO royalties: terms

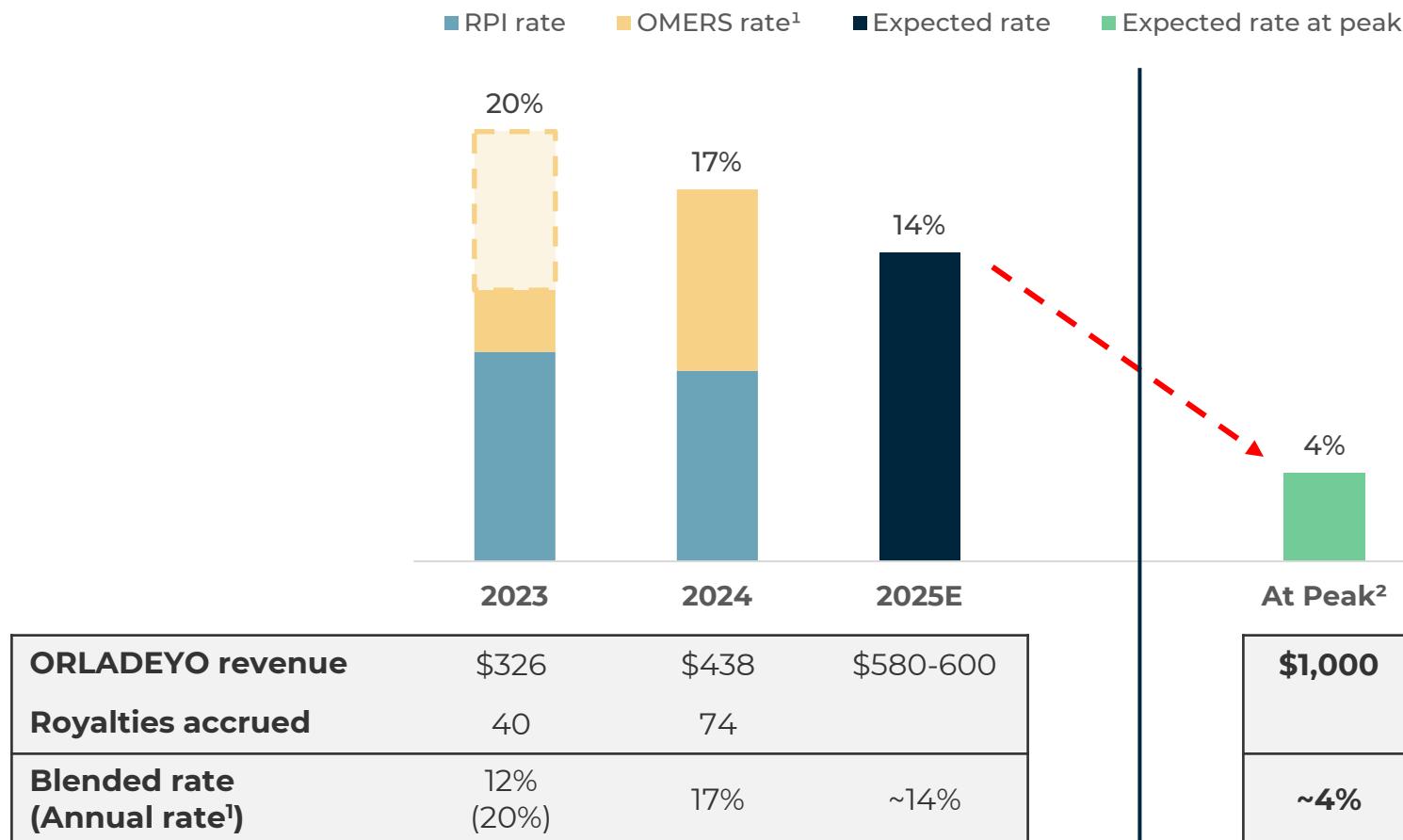
	Upfront	Rate Tiers (Direct ²)	Rate Tiers (Indirect)	Cumulative Payback Cap
RP 2020	\$125M	\$0-350M: 8.75% \$350M-550M: 2.75% Over \$550M: None	\$0-150M: 20% \$150M-230M: 10% Over \$230M: None	None
RP 2021	\$150M ¹	\$0-350M: 0.75% \$350M-550M: 1.75% Over \$550M: None	\$0-150M: 3% \$150M-230M: 2% Over \$230M: None	None
OMERS 2021	\$150M	\$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. Direct sales include the United States, key European markets and other markets where ORLADEYO is sold directly or through distributors.

ORLADEYO royalty rate now declining

(Figures in millions)



- We expect total royalties to be steady and blended rate to decline through peak, now that revenue has reached royalty free tier (>\$550M)
- Rate expected to settle ~4% at peak once OMERS reaches cap

1. The company began making royalty payments to OMERS in 4Q 2023. Annual rate is defined here as the royalty rate that would be applied if royalties were accrued on a full year basis using the current rate schedule.

2. Example calculation assumes only direct sales, that that OMERS royalty has reached its cap, and is for illustrative purposes only.

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