Third Quarter 2024 Results Call

Corporate Update & Financial Results

November 4, 2024

Forward-looking statements

BioCryst's presentation contains forward-looking statements, including statements regarding future results, unaudited and forward-looking financial information and company performance, achievements, or future market share. These statements are subject to known and unknown risks, uncertainties and other factors which may cause our actual results, performance, achievements, or market share to be materially different from any future results, performance, achievements, or market share expressed or implied in this presentation. These statements reflect our current views with respect to future events and are based on assumptions and are subject to risks and uncertainties.

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.

AGENDA

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

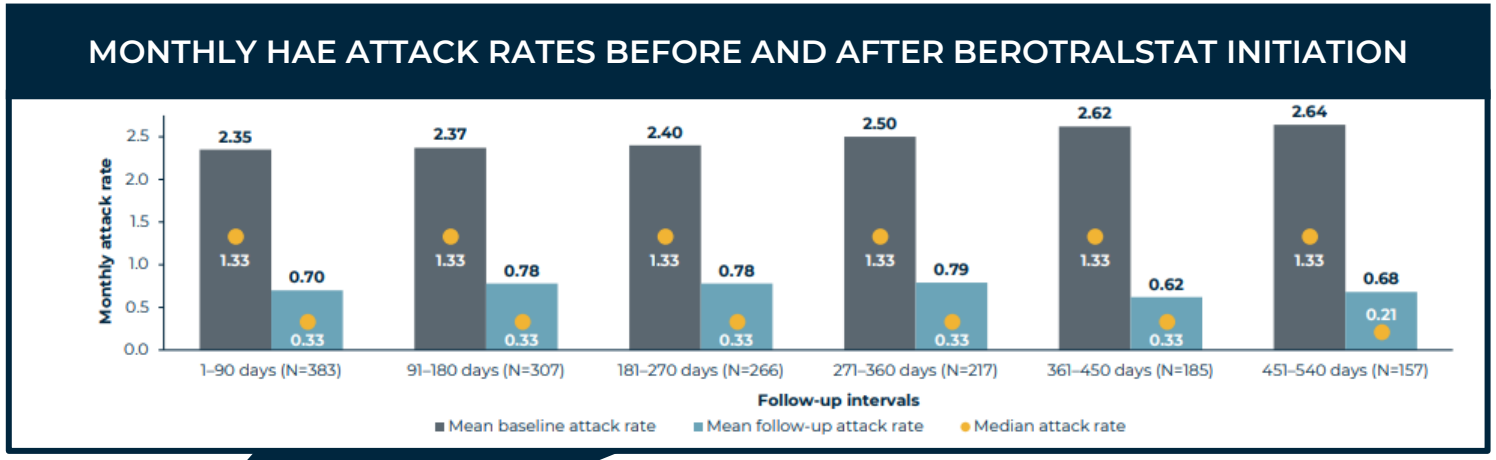
Strong ORLADEYO growth and business progress continues in Q3

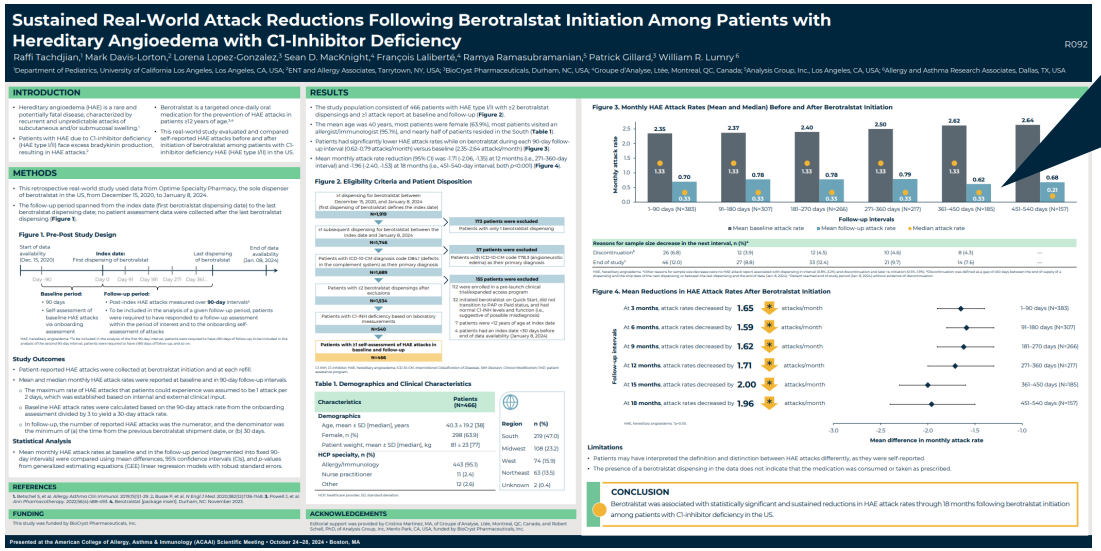
COMMERCIAL	• ORLADEYO revenue of $116.3m (+35.7% y/y) • Full year ORLADEYO guidance raised to $430-435m (from $420-435m) • Introduced total product revenue guidance $443-448m (including additional 2024 RAPIVAB revenue)
CLINICAL	• ORLADEYO pediatric study APeX-P is fully enrolled and on track for regulatory submission in 2025 • BCX17725 advanced into clinic with first enrolled participant in Phase 1 study • Initial patient data expected by end of 2025 • Avoralstat remains on track to enter clinic in 2025 with initial patient data by end of 2025

FINANCIAL	• Second consecutive quarter of GAAP operating profit (+$7.7m, +$24.9m non-GAAP)
	• On track for full-year 2024 non-GAAP operating profit
	• Due to our strong financial position and capital markets independence, we elected:
	  – Not to draw additional $150m tranche of Pharmakon debt
	  – Not to exercise Q3 PIK option on Pharmakon interest

REAL WORLD EVIDENCE: Type 1 and 2 HAE patients 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

R092

Raffi Tachdjian,[1] Mark Davis-Lorton,[2] Lorena Lopez-Gonzalez,[3] Sean D. MacKnight,[4] François Laliberté,[4] Ramya Ramasubramanian,[5] Patrick Gillard,[3] William R. Lumry[6]

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INTRODUCTION

- Hereditary angioedema (HAE) is a rare and potentially fatal disease, characterized by recurrent and unpredictable attacks of subcutaneous and/or submucosal swelling[1]
- Patients with HAE due to C1-inhibitor deficiency (HAE type I/II) face excess bradykinin production, resulting in HAE attacks.[2]
- Berotralstat is a targeted once-daily oral medication for the prevention of HAE attacks in patients ≥12 years of age.[3,4]
- This real-world study evaluated and compared self-reported HAE attacks before and after initiation of berotralstat among patients with C1-inhibitor deficiency HAE (HAE type I/II) in the US.

METHODS

- This retrospective real-world study used data from Optime Specialty Pharmacy, the sole dispenser of berotralstat in the US, from December 15, 2020, to January 8, 2024.
- The follow-up period spanned from the index date (first berotralstat dispensing date) to the last berotralstat dispensing date; no patient assessment data were collected after the last berotralstat dispensing (**Figure 1**).

Figure 1. Pre-Post Study Design

Study Outcomes

- Patient-reported HAE attacks were collected at berotralstat initiation and at each refill.
- Mean and median monthly HAE attack rates were reported at baseline and in 90-day follow-up intervals.
  - The maximum rate of HAE attacks that patients could experience was assumed to be 1 attack per 2 days, which was established based on internal and external clinical input.
  - Baseline HAE attack rates were calculated based on the 90-day attack rate from the onboarding assessment divided by 3 to yield a 30-day attack rate.
  - In follow-up, the number of reported HAE attacks was the numerator, and the denominator was the minimum of (a) the time from the previous berotralstat shipment date, or (b) 30 days.

Statistical Analysis

- Mean monthly HAE attack rates at baseline and in the follow-up period (segmented into fixed 90-day intervals) were compared using mean differences, 95% confidence intervals (CIs), and p-values from generalized estimating equations (GEE) linear regression models with robust standard errors.

RESULTS

- The study population consisted of 466 patients with HAE type I/II with ≥2 berotralstat dispensings and ≥1 attack report at baseline and follow-up (**Figure 2**).
- The mean age was 40 years, most patients were female (83.9%), most patients visited an allergist/immunologist (55.1%), and nearly half of patients resided in the South (**Table 1**).
- Patients had significantly lower HAE attack rates while on berotralstat during each 90-day follow-up interval (0.62–0.79 attacks/month) versus baseline (2.35–2.64 attacks/month) (**Figure 3**).
- Mean monthly attack rate reduction (95% CI) was -1.71 (-2.06, -1.35) at 12 months (i.e., 271–360-day interval) and -1.96 (-2.40, -1.53) at 18 months (i.e., 451–540-day interval; both p<0.001) (**Figure 4**).

Figure 2. Eligibility Criteria and Patient Disposition

Table 1. Demographics and Clinical Characteristics

Characteristics	Patients (N=466)
Demographics	
Age, mean ± SD [median], years	40.3 ± 19.2 [38]
Female, n (%)	298 (63.9)
Patient weight, mean ± SD [median], kg	81 ± 23 [77]
HCP specialty, n (%)	
Allergy/Immunology	443 (95.1)
Nurse practitioner	11 (2.4)
Other	12 (2.6)

Region	n (%)
South	219 (47.0)
Midwest	108 (23.2)
West	74 (15.9)
Northeast	63 (13.5)
Unknown	2 (0.4)

HCP, healthcare provider; SD, standard deviation.

Figure 3. Monthly HAE Attack Rates (Mean and Median) Before and After Berotralstat Initiation

Reasons for sample size decrease in the next interval, n (%)[a]

	1–90 days (N=383)	91–180 days (N=307)	181–270 days (N=266)	271–360 days (N=217)	361–450 days (N=185)
Discontinuation[b]	26 (6.8)	12 (3.9)	12 (4.5)	10 (4.6)	8 (4.3)
End of study[c]	46 (12.0)	27 (8.8)	33 (12.4)	21 (9.7)	14 (7.6)

HAE, hereditary angioedema. [a]Other reasons for sample size decrease were in HAE attack reports associated with dispensing in interval (0.8%–2.3%) and discontinuation and later re-initiation (0.0%–1.9%). [b]Discontinuation was defined as a gap of ≥60 days between the end of supply of a dispensing and the first date of the next dispensing, or between the last dispensing and the end of data (Jan. 8, 2024). [c]Patient reached end of study period (Jan. 8, 2024) without evidence of discontinuation.

Figure 4. Mean Reductions in HAE Attack Rates After Berotralstat Initiation

HAE, hereditary angioedema.

Limitations

- Patients may have interpreted the definition and distinction between HAE attacks differently, as they were self-reported.
- The presence of a berotralstat dispensing in the data does not indicate that the medication was consumed or taken as prescribed.

CONCLUSION

Berotralstat was associated with statistically significant and sustained reductions in HAE attack rates through 18 months following berotralstat initiation among patients with C1-inhibitor deficiency in the US.

REFERENCES

1. Betschel S, et al. Allergy Asthma Clin Immunol. 2019;15(1):29. 2. Busse P, et al. N Engl J Med. 2022;386(12):1134-1148. 3. Powell J, et al. Ann Pharmacother. 2022;56(4):488-499. 4. Berotralstat [package insert]. Durham, NC: November 2023.

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ACKNOWLEDGEMENTS

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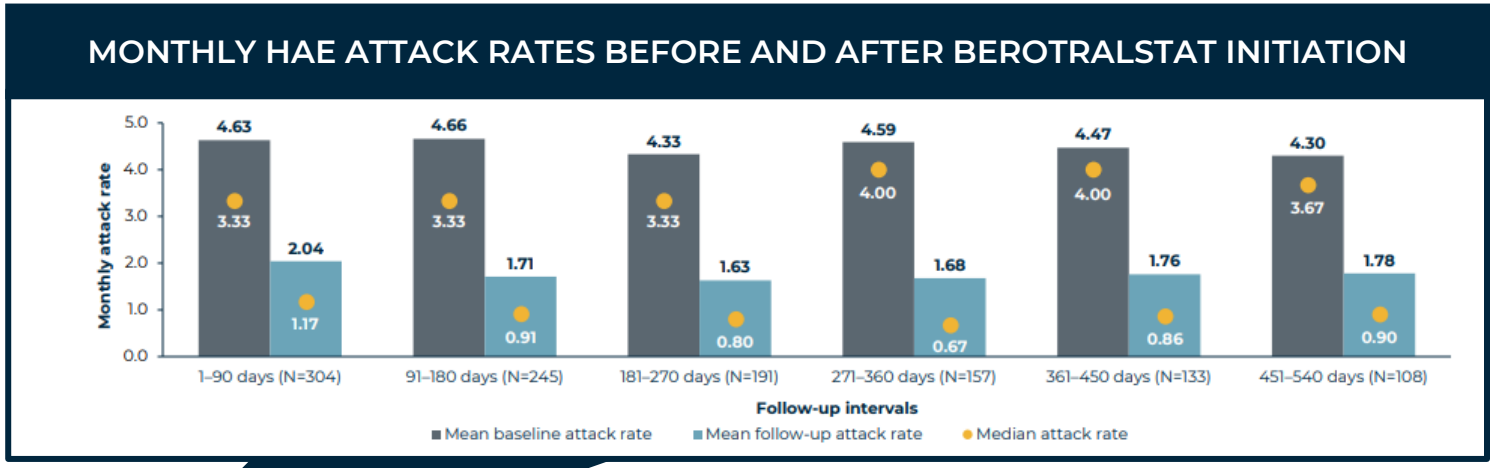
Presented at the American College of Allergy, Asthma & Immunology (ACAAI) Scientific Meeting • October 24–28, 2024 • Boston, MA

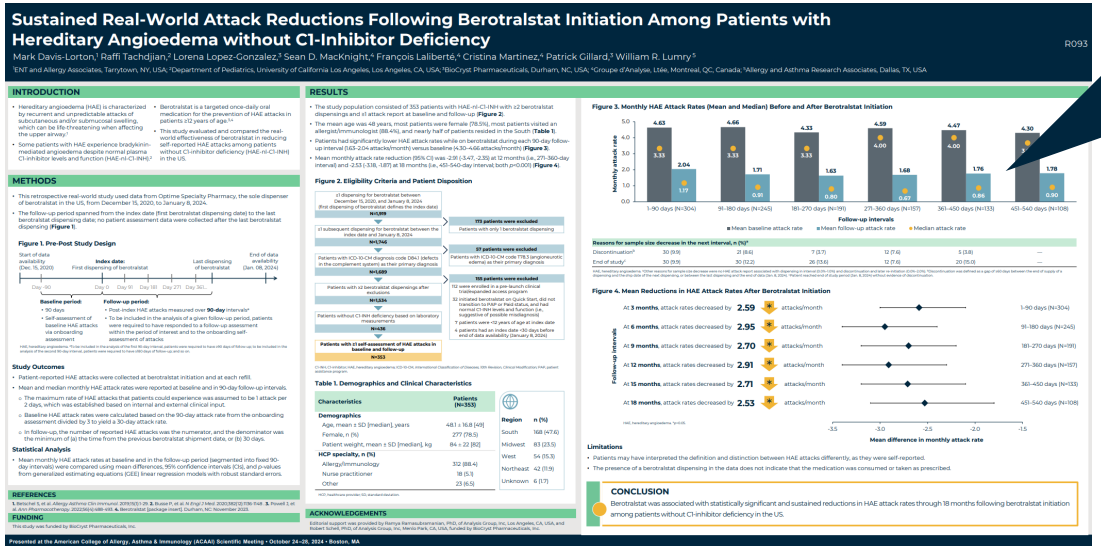
- The primary reason for reduced patient counts over time was that patients had not been on ORLADEYO long enough to be evaluated at all time points
- Only 68 (14.6%) out of 466 patients in this study discontinued therapy

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

REAL WORLD EVIDENCE: C1 normal-inh HAE patients 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 Berotralstat Initiation Among Patients with Hereditary Angioedema without C1-Inhibitor Deficiency

R093

Mark Davis-Lorton,[1] Raffi Tachdjian,[2] Lorena Lopez-Gonzalez,[3] Sean D. MacKnight,[4] François Laliberté,[4] Cristina Martinez,[4] Patrick Gillard,[3] William R. Lumry[5]

[1]ENT and Allergy Associates, Tarrytown, NY, USA; [2]Department of Pediatrics, University of California Los Angeles, Los Angeles, CA, USA; [3]BioCryst Pharmaceuticals, Durham, NC, USA; [4]Groupe d'Analyse, Ltée, Montreal, QC, Canada; [5]Allergy and Asthma Research Associates, Dallas, TX, USA

INTRODUCTION

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RESULTS

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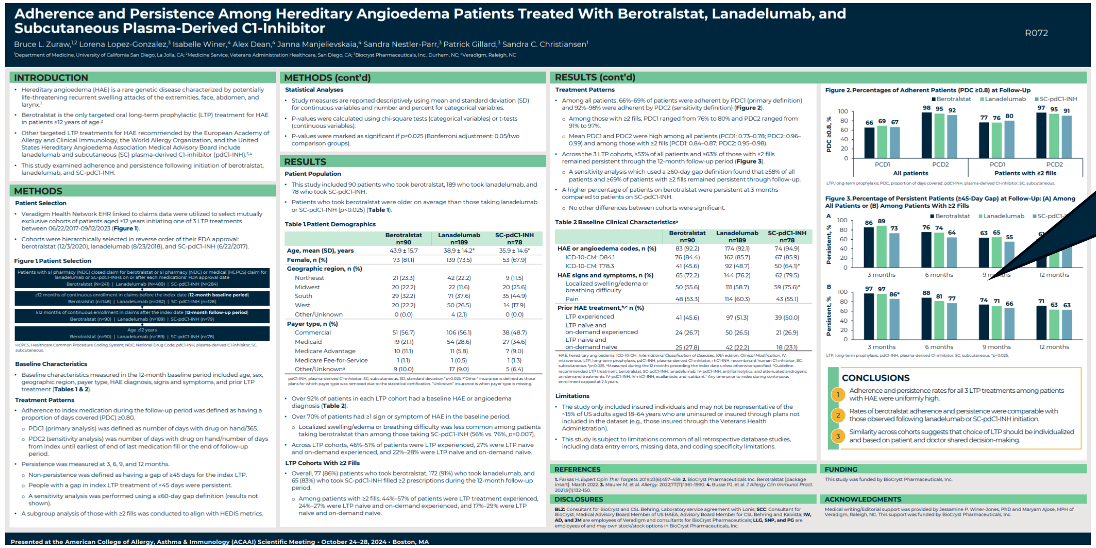
- The primary reason for reduced patient counts over time was that patients had not been on ORLADEYO long enough to be evaluated at all time points
- Only 75 (21.2%) out of 353 patients in this study discontinued therapy

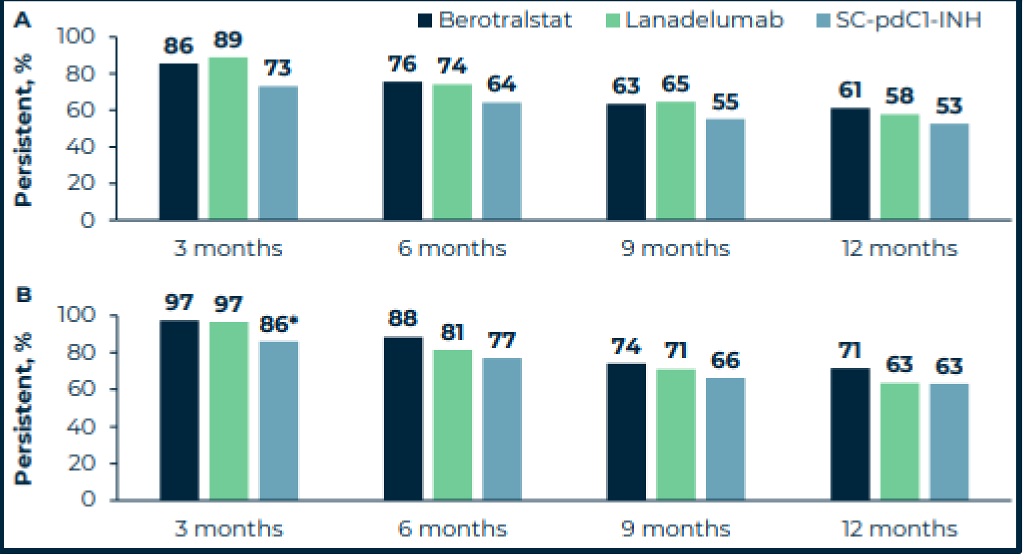
Source: Sustained Real-World Attack Reductions Following Berotralstat Initiation Among Patients with Hereditary Angioedema without C1-Inhibitor Deficiency
Presented at the ACAAI Scientific Meting 2024 • October 24-28, 2024

REAL WORLD EVIDENCE: ORLADEYO persistence is not different from other LTP products

- Adherence and persistence rates for all three LTP treatments among patients with HAE were uniformly high
- Rates of ORLADEYO adherence and persistence were comparable with those observed following lanadelumab or SC-pdC1-INH initiation

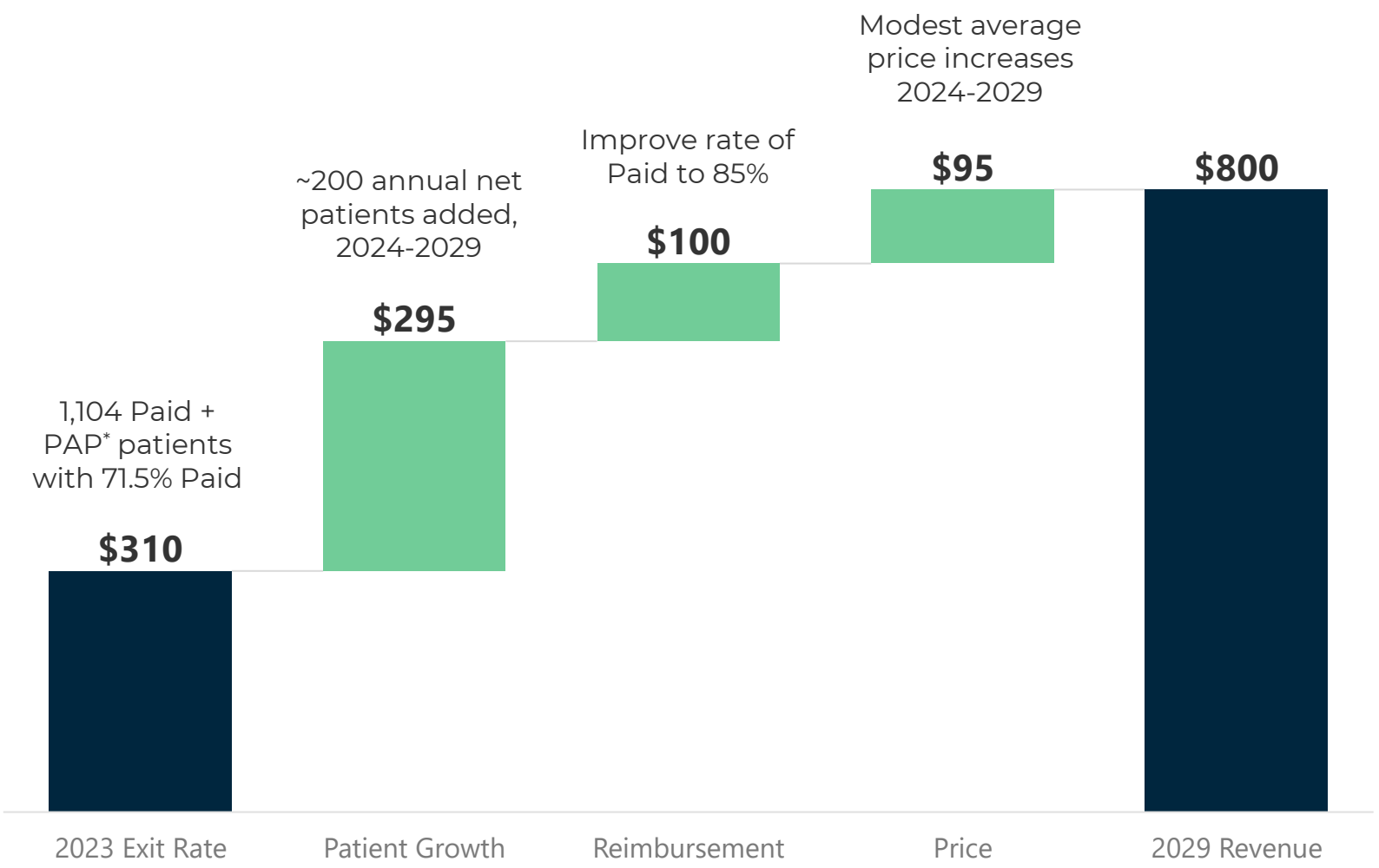


PERCENTAGE OF PERSISTENT PATIENTS (≥45-DAY GAP) AT FOLLOW-UP: (A) AMONG ALL PATIENTS OR (B) AMONG PATIENTS WITH ≥2 FILLS



Source: Adherence and Persistence Among Hereditary Angioedema Patients Treated With Berotralstat, Lanadelumab, and Subcutaneous Plasma-Derived C1-Inhibitor
Presented at the ACAAI Scientific Meting 2024 · October 24-28, 2024

Path to $800M US revenue in 2029



ASSUMPTIONS

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

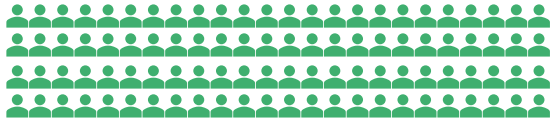
* PAP is the company's long-term patient assistance program

Comprehensive annual research + market simulation

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

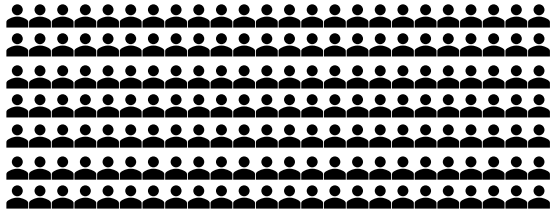
Research Sample*

PATIENTS



n=100 HAE patients

PHYSICIANS



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

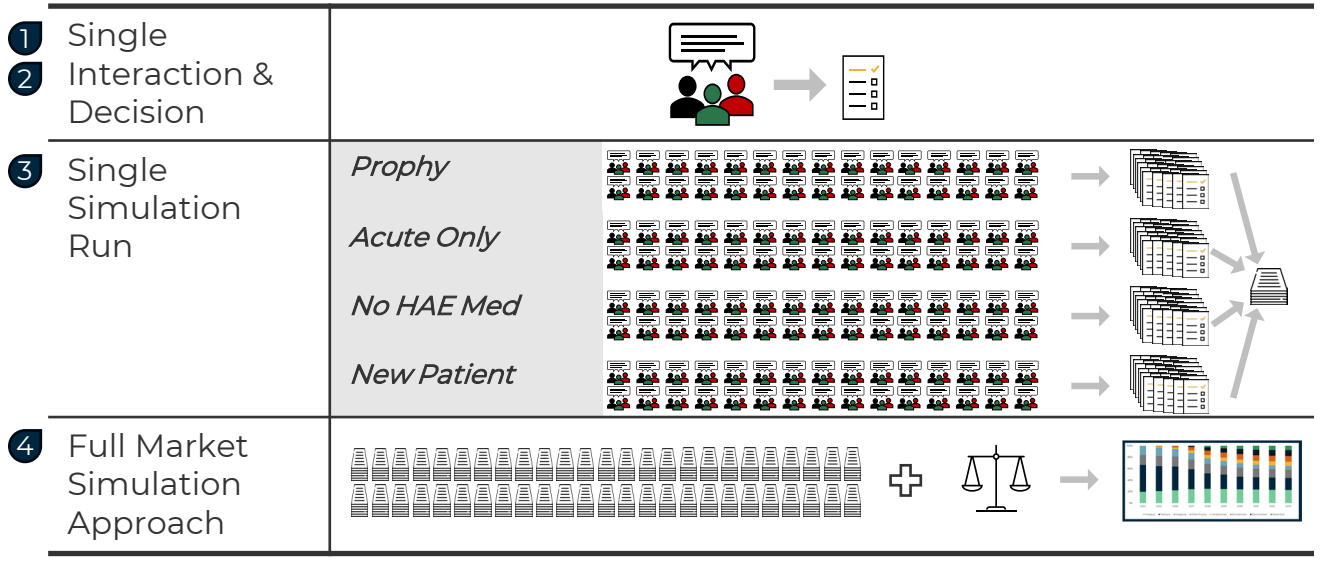
PAYERS

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

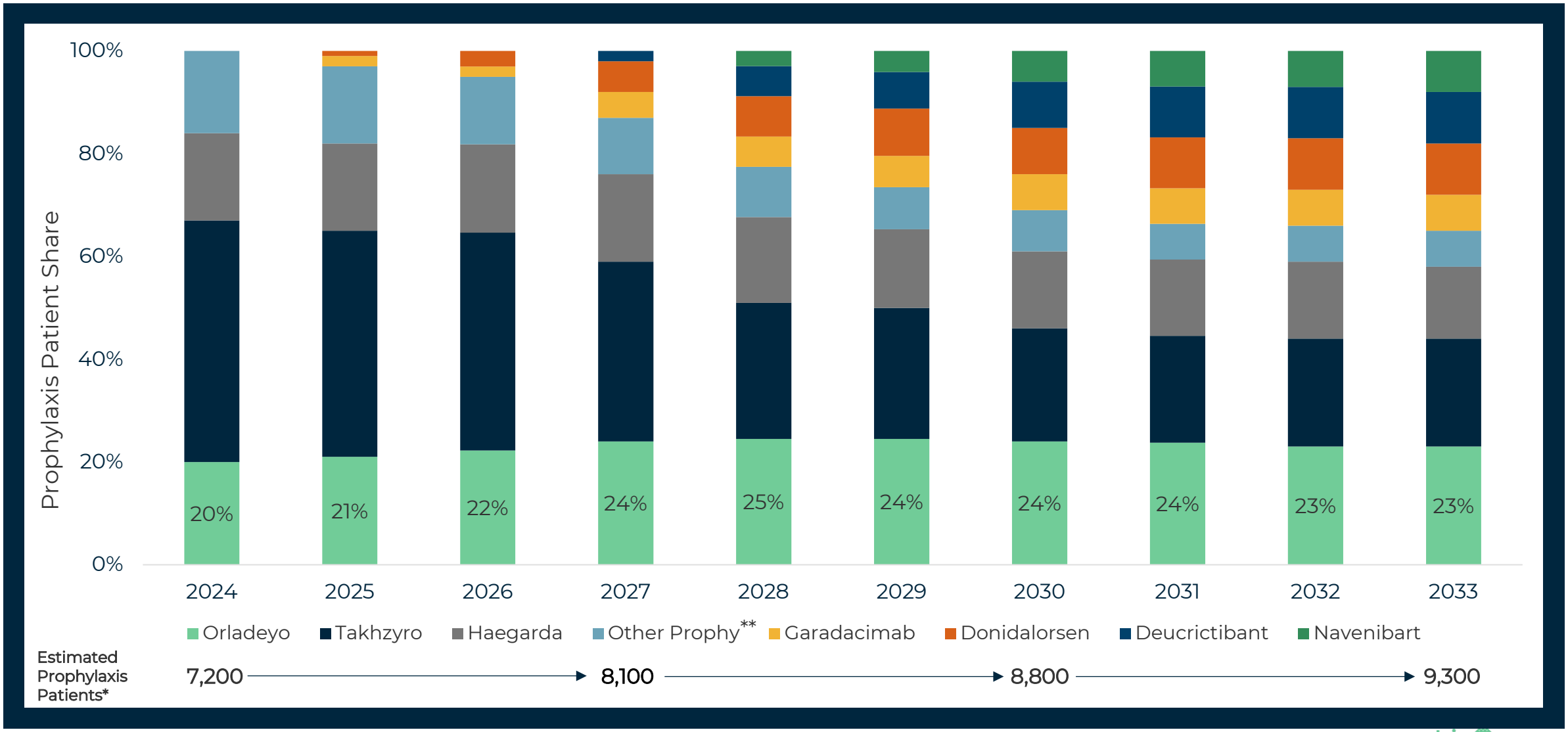
Modeling Process - Visual Example



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

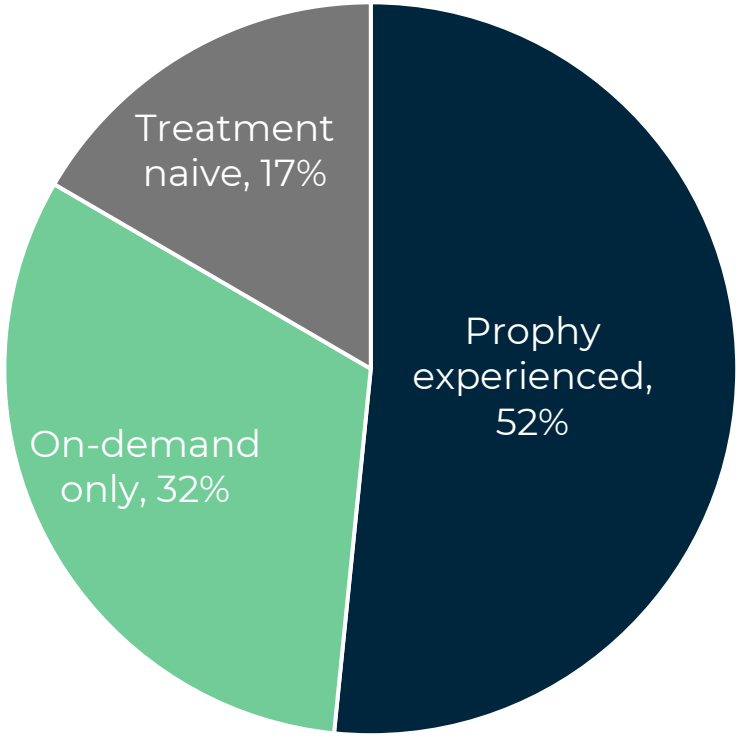
Monte Carlo simulation outcome: U.S. prophy market share

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



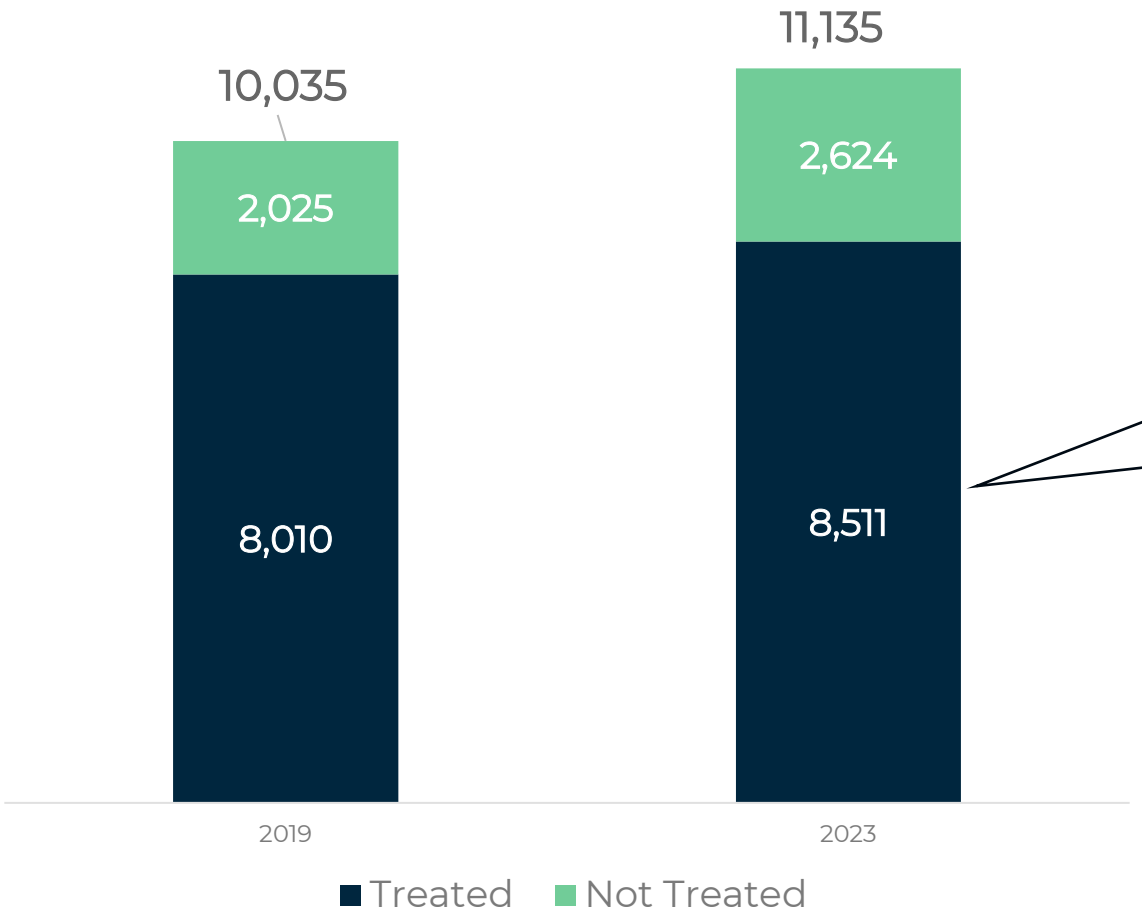
Source: BioCryst Internal Market Research Study (Conducted Jun 2024) *Source: 2018-2023 administrative claims data
**Other Prophy: Any other current medication (including acute) taken prophylactically for HAE

Over 50% of patients trying ORLADEYO launch-to-date had prior experience on another prophy therapy



Source: Specialty Pharmacy patient-reported data through June 3, 2024, supplemented with 2015-2024 administrative claims data.

The HAE market of diagnosed and treated patients continues to grow



Between 2019 and 2023:

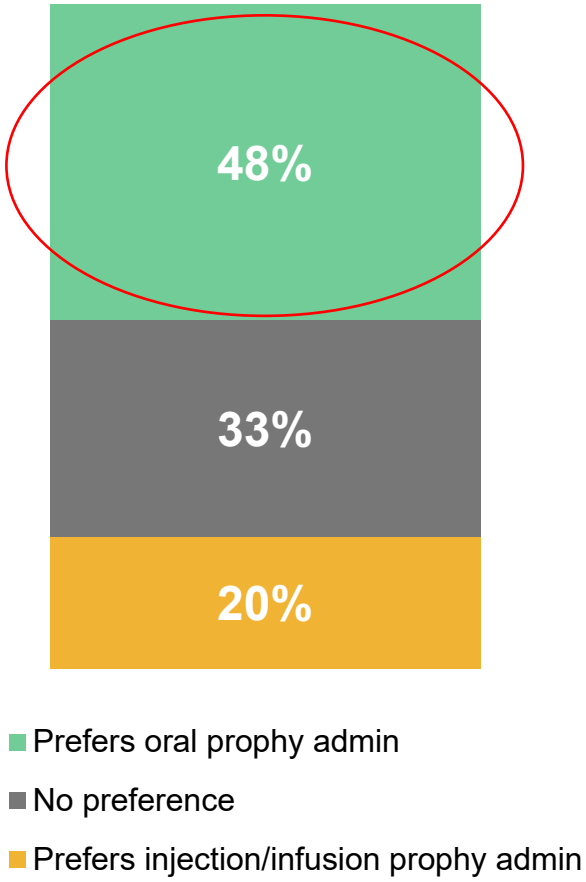
- Over 1,000 more diagnosed patients
- Over 500 more patients treated for HAE

Source: 2018-2023 administrative claims data

MARKET RESEARCH: 1 in 2 injectable prophy users prefers oral ROA, 3 in 4 are willing to switch

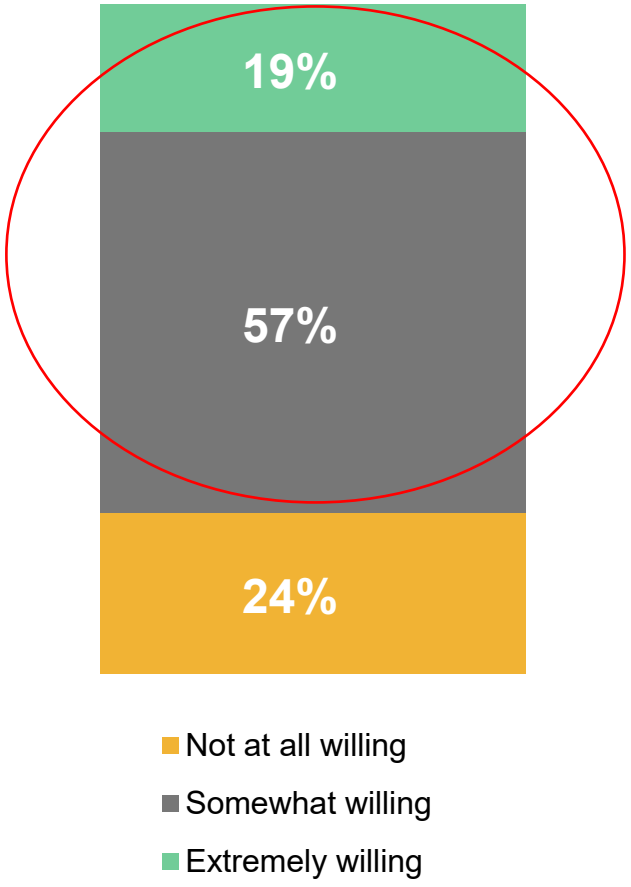
PREFERENCE AMONG CURRENT INJECTABLE PROPHY USERS

(n=120)



WILLINGNESS TO SWITCH HAE LTP AMONG CURRENT INJECTABLE PROPHY USERS

(n=120)



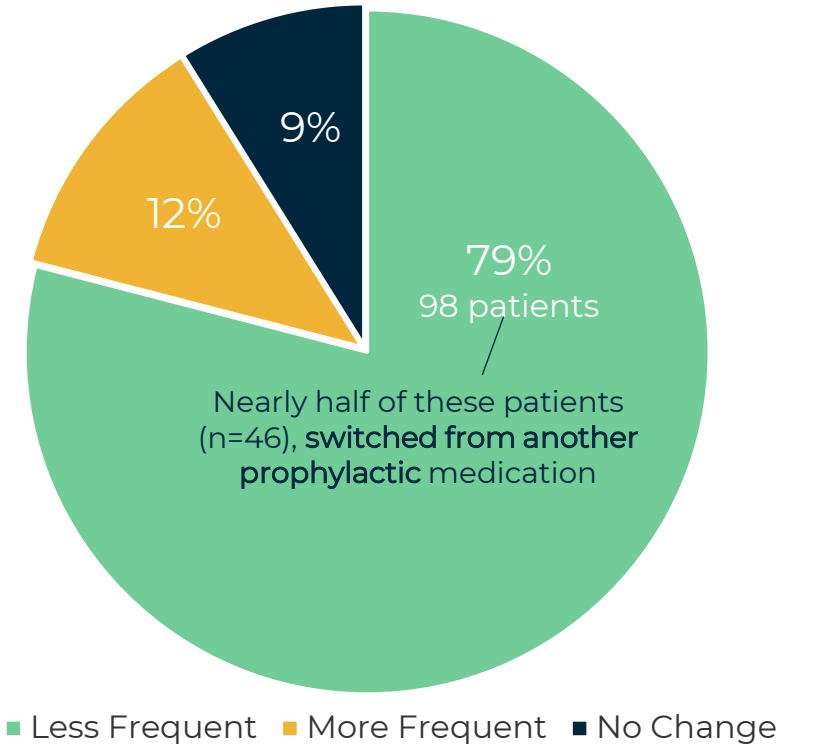
Source: BioCryst Internal Market Research Study (Conducted Oct 2023)

ROA = route of administration
LTP = long-term prophylaxis

MARKET RESEARCH: 4 out of 5 patients report having fewer attacks after starting ORLADEYO and 3 out of 4 report less severe attacks

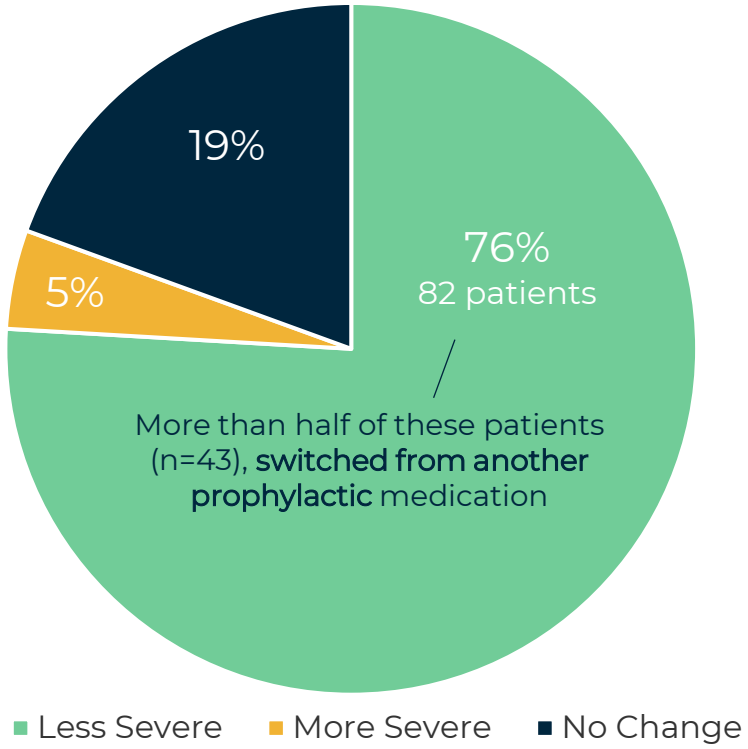
HAE ATTACK FREQUENCY ON ORLADEYO

All Respondents (n=124)



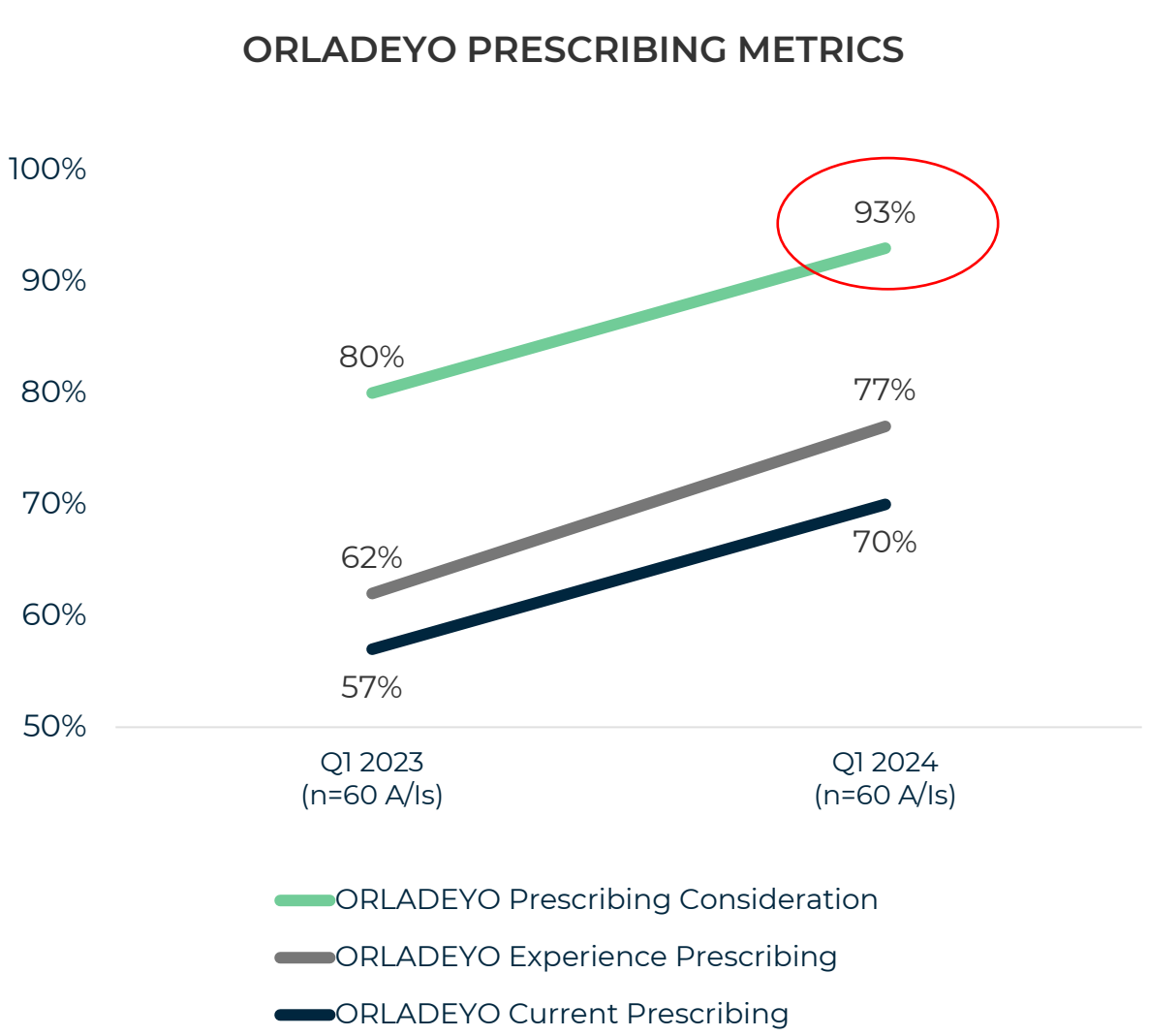
HAE ATTACK SEVERITY ON ORLADEYO

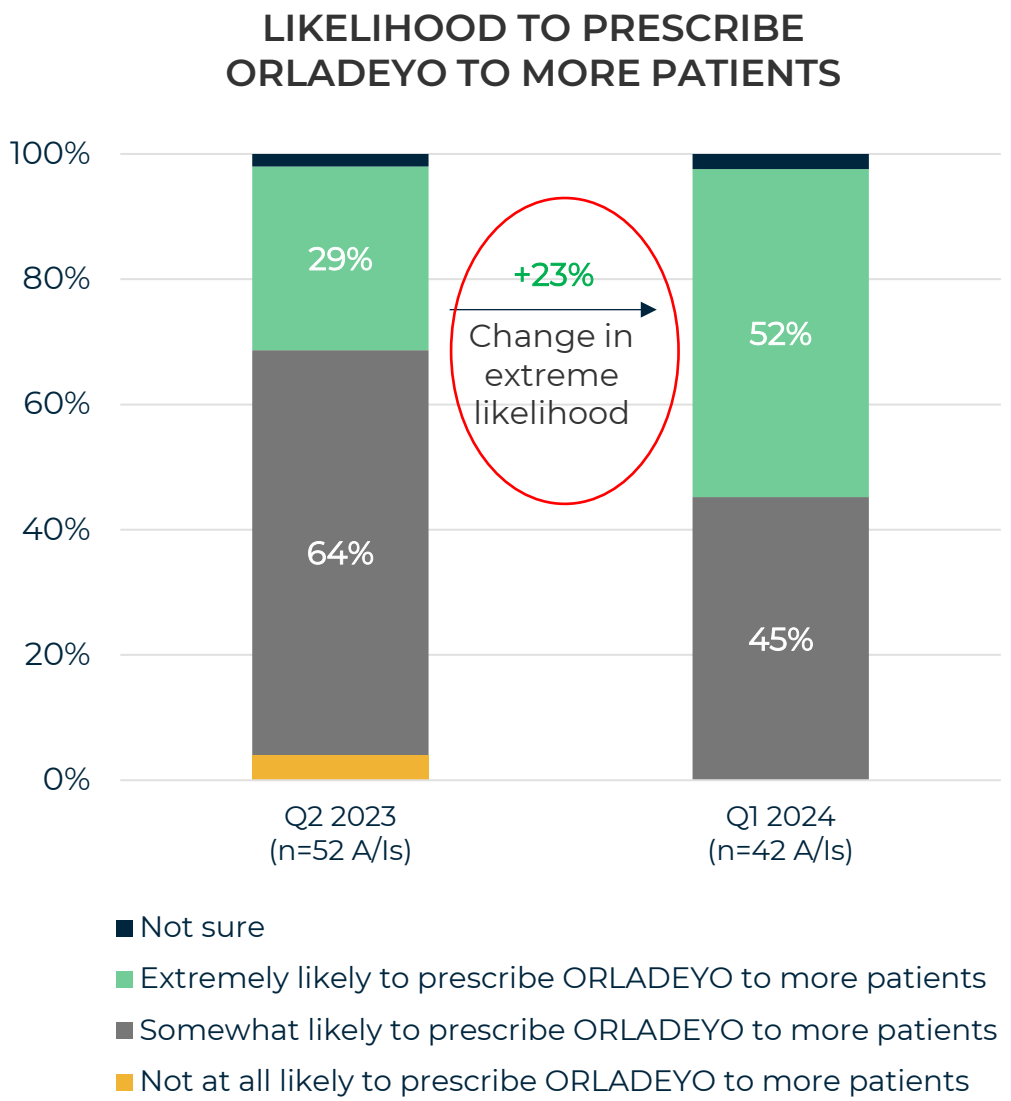
All Respondents (n=108)



Source: BioCryst Internal Market Research Studies (Conducted Jan 2023, Apr 2024)

MARKET RESEARCH: Allergist/Immunologist intent to prescribe has increased strongly since the first half of 2023





Source: BioCryst Internal Market Research Studies (Conducted Feb-Mar 2023, May 2023, Feb 2024)

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.

BCX17725 Phase 1 enrollment begins

ASSET	2024	2025	2026	2027	2028
BCX17725 Protein Therapeutic	Start Phase 1	Start POC	POC data		

Next catalyst: initial patient data by end of 2025

What is Netherton syndrome?

- A severe, rare, genetic skin condition, caused by a loss-of-function mutation in SPINK5 gene
- SPINK5 is a natural inhibitor of KLK5, a serine protease that regulates skin turnover
- Lack of KLK5 inhibition is the underlying cause of disease
- Causes full-body redness, inflammation, infection risk, itching, fragile hair, and high infant mortality

Market opportunity

Population
- Estimated 1,600 in US based on claims analysis
- Up to 5,000 with improved diagnosis (no existing ICD code)

Competition
- No approved disease-modifying therapies

Pricing
- Typical pricing for rare disease

BCX17725 is a highly specific fusion protein KLK5 inhibitor that targets the underlying cause of disease

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

2024 FY GUIDANCE	
ORLADEYO revenue	$430-435
Total product revenue	$443-448
Operating expenses (excluding non-cash comp)	$380-390

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	• 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

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.

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