

BioCryst Pharmaceuticals, Inc.

Corporate Presentation

September 2023



ORLADEYO® (berotralstat) PROVIDES SUSTAINED ATTACK RATE REDUCTION¹

Patients who completed 96 weeks of treatment saw sustained reductions in their HAE attack rates, demonstrating the durability of ORLADEYO

21 patients who were randomized to ORLADEYO 150 mg at the beginning of APeX-2 and completed 96 weeks of treatment demonstrated a decline in mean attack rate per 4 weeks from baseline to 96 weeks of treatment^b

SEM, standard error of mean.

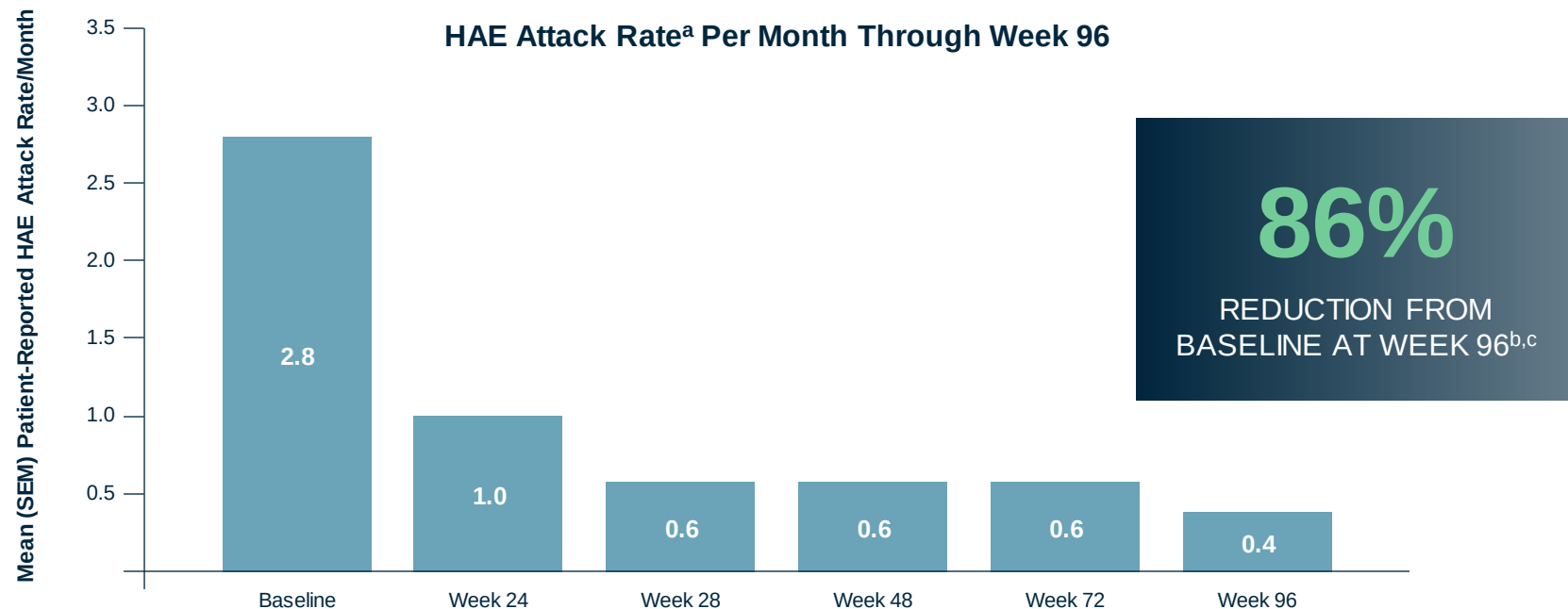
^aDue to study design, investigator-confirmed attack rates were reported only during the first 48 weeks, while patient-reported attack rates were reported during weeks 49 to 96. For consistency across the entire 96 weeks, only patient-reported attack rates are reported. For analysis purposes, 1 month was defined as 4 weeks of treatment.¹

^bThis reflects an ad hoc analysis of interim data.^{1,2}

^c86% attack rate reduction from baseline to week 96 was seen for patients who completed 96 weeks of treatment with ORLADEYO 150 mg (n = 21).¹

1. Kiani S, et al. Presented at: European Academy of Allergy and Clinical Immunology Hybrid Congress; July 10-12, 2021.

2. Data on file, BioCryst Pharmaceuticals, Inc.



IN 16 OF THE LAST 17 MONTHS OF TREATMENT, MEDIAN ATTACK RATE WAS 0 ATTACKS PER MONTH^b

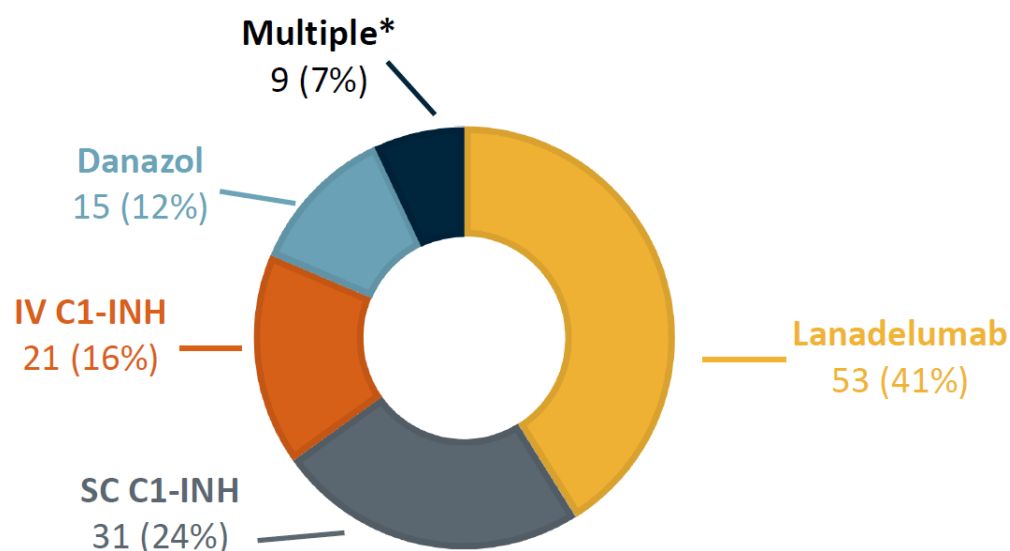
SELECT IMPORTANT SAFETY INFORMATION

The most common adverse reactions (≥10% and higher than placebo) in patients receiving ORLADEYO were abdominal pain, vomiting, diarrhea, back pain, and gastroesophageal reflux disease.

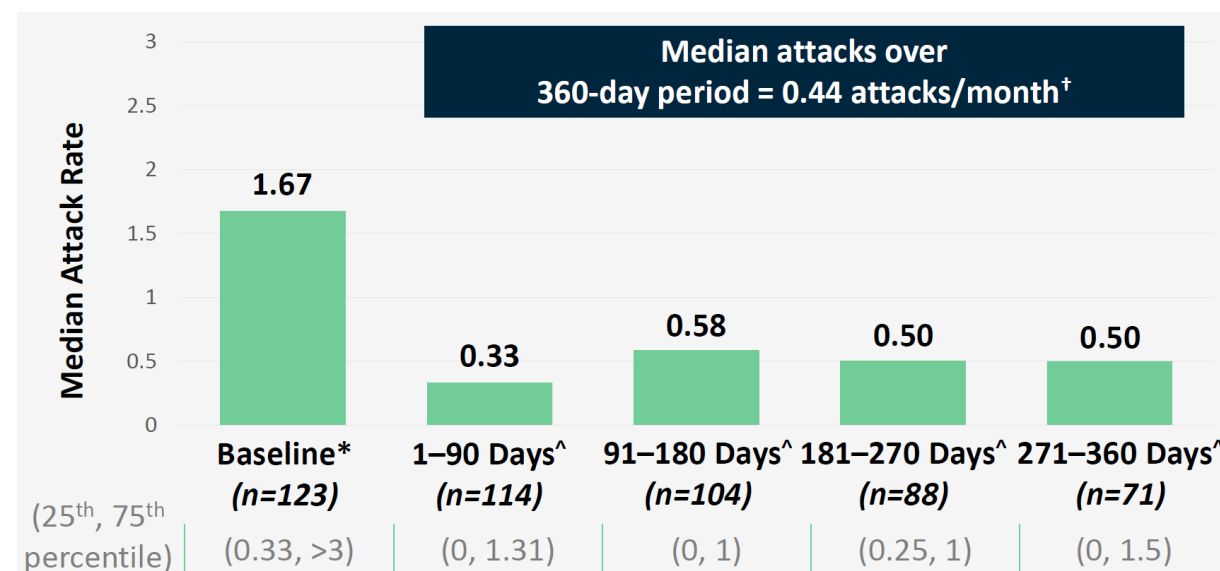
Please see Important Safety Information.

ACAAI: ORLADEYO Real-World Data Show Sustained Reduction in Attacks, Regardless of Prior Therapy¹

Patient distribution of prophylactic therapies prior to berotralstat (n (%))



Monthly median attack rates in patients with prior prophylaxis who initiated berotralstat



The reduction in median attack rates* from baseline over the 1-360 days period was consistent for each prior prophylaxis

- **Lanadelumab: 77% reduction** from baseline (1 attacks/month) to average rate over days 1-360 of 0.23 attacks/month
- **SC C1-INH: 64% reduction** from baseline (1.83 attacks/month) to average rate over days 1-360 of 0.67 attacks/month
- **Danazol: 70% reduction** from baseline (1.67 attacks/month) to average rate over days 1-360 of 0.5 attacks/month
- **IV C1-INH: 72% reduction** from baseline (2.17 attacks/month) to average rate over days 1-360 of 0.62 attacks/month

*Percent reduction vs. baseline compares the median baseline attack rate to the median patient attack rate on berotralstat. The median attack rate on berotralstat is the median of the average attack rate over the 360-day period for each patient. The average attack rate for each patient was determined by taking the average of all the attack rates reported for each patient.

Safety: Adverse events were reported in 44/129 (34%) patients

Approved Label: ORLADEYO® (berotralstat) Safety

In APeX-2 (part 1), the most common^a treatment-emergent adverse reactions were abdominal pain, vomiting, diarrhea, back pain, and gastroesophageal reflux disease (GERD)

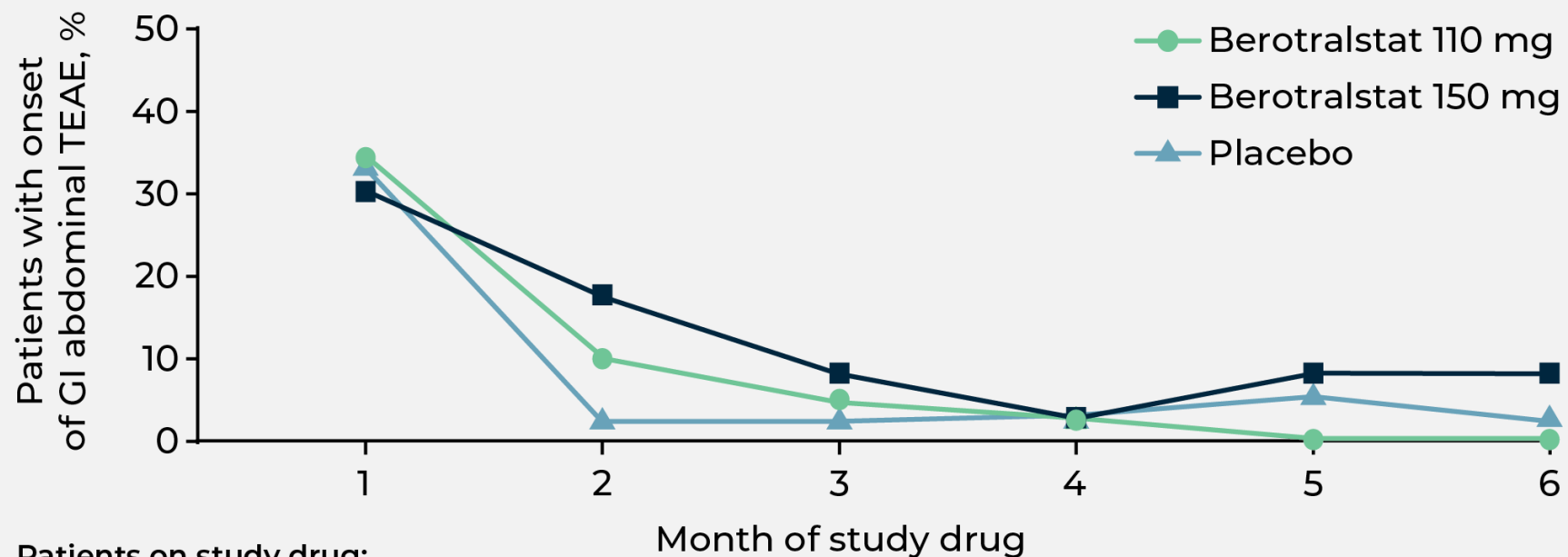
Adverse reactions	Placebo (n=39)	ORLADEYO 110 mg (n=41)	ORLADEYO 150 mg (n=40)
	n (%)	n (%)	n (%)
Abdominal pain ^b	4 (10)	4 (10)	9 (23)
Vomiting	1 (3)	4 (10)	6 (15)
Diarrhea ^c	0	4 (10)	6 (15)
Back pain	1 (3)	1 (2)	4 (10)
GERD	0	4 (10)	2 (5)

^a≥10% and higher than placebo. ^bIncludes abdominal pain, abdominal discomfort, abdominal tenderness, and upper abdominal pain. ^cIncludes diarrhea and frequent bowel movements.

Findings from the open-label, long-term safety study, APeX-S (interim safety population, n=227), support the data observed in APeX-2 (part 1)

Incidence of GI Abdominal AEs Declines Quickly After First Month

Incidence of New-Onset GI Abdominal AEs by Month



Patients on study drug:

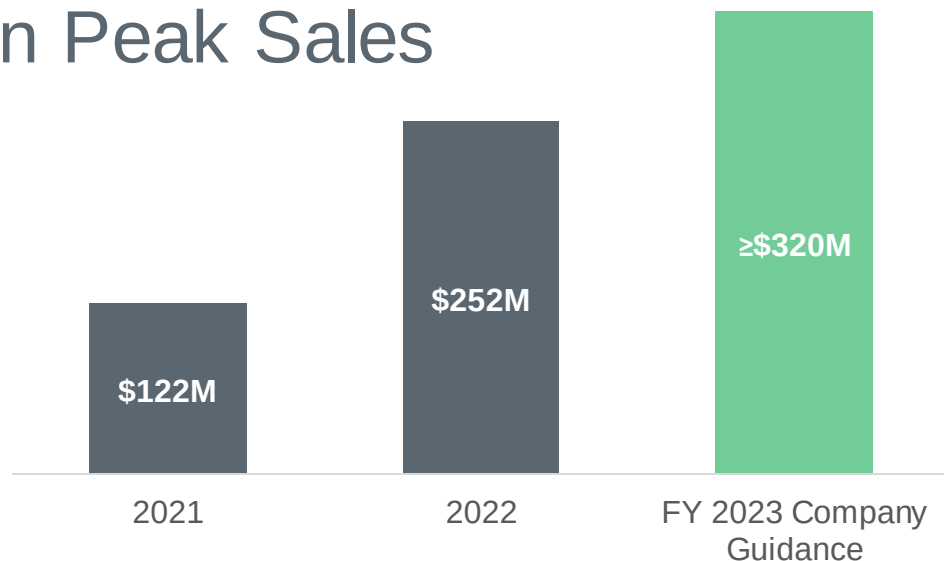
Berotralstat 110 mg	41	41	41	41	40	38
Berotralstat 150 mg	40	40	37	37	37	37
Placebo	39	39	38	37	36	34

GI=gastrointestinal; TEAE=treatment-emergent adverse event.

APeX-2 ata Presented at Annual Meeting of the American Academy of Allergy Asthma & Immunology Annual, March 2020

Exceptional Launch and on a Path to \$1 Billion Peak

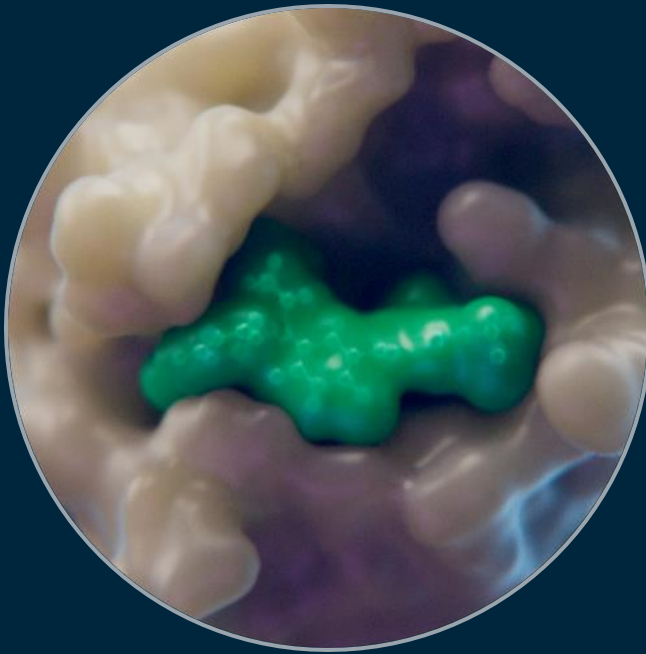
ORLADEYO:
\$1 Billion
in Peak Sales



Key Highlights

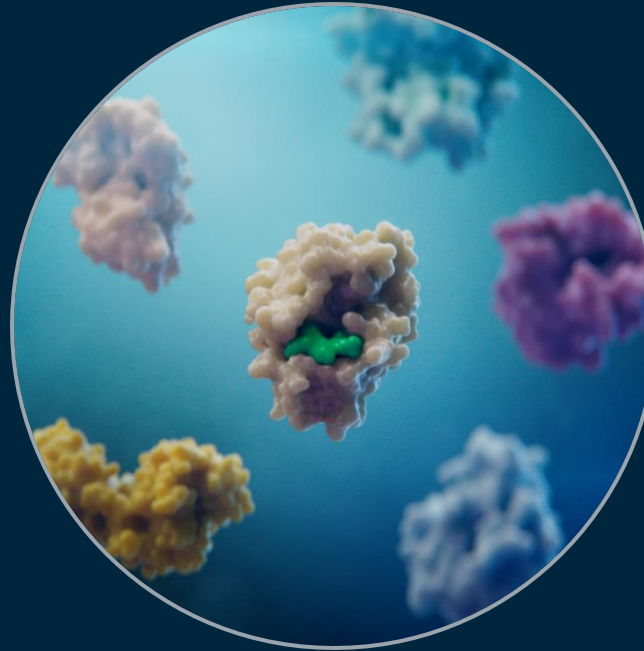
- >25% to peak global sales of \$1B after second year of launch
- To achieve \$1B in peak sales, need 25%-30% U.S. share
 - \$800M in U.S.
 - \$200M in Europe/RoW
- Composition of matter patent protection into 2039

3 Critical Factors for Successful Drug Design



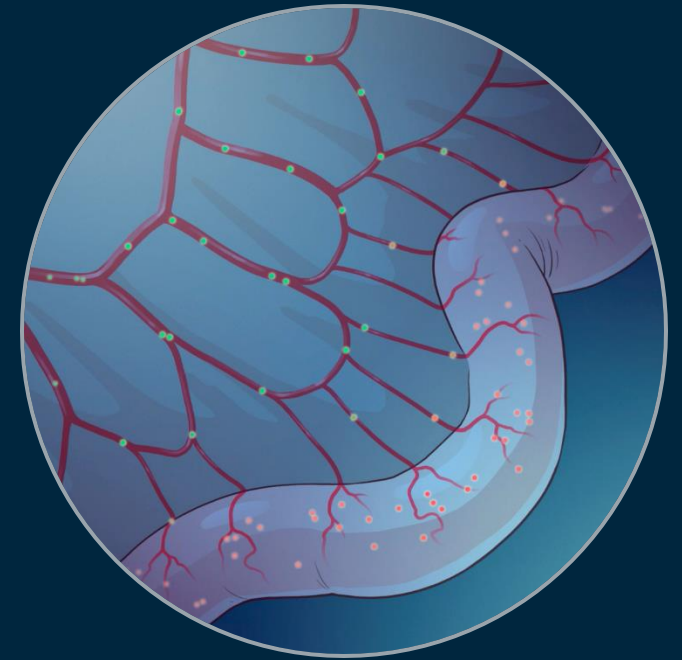
Potency

Needs to bind physically and electrostatically to inhibit an ever-changing target¹⁻³



Selectivity

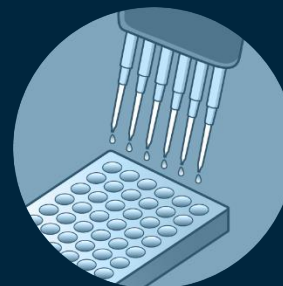
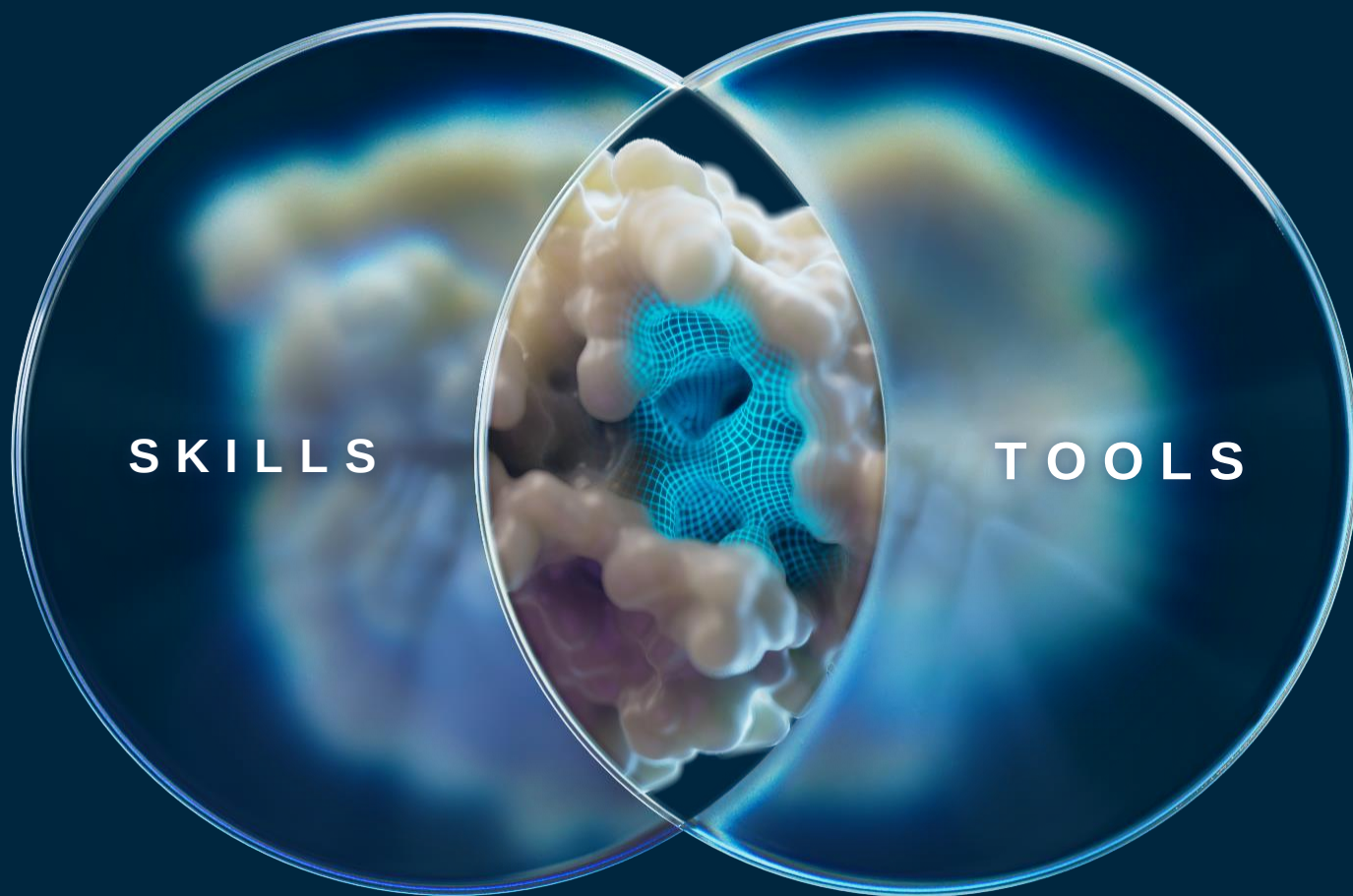
Needs unique, identifiable features that inhibit a specific serine protease⁴



Bioavailability

Oral molecules need to be soluble to cross from the GI tract into the bloodstream⁵

BioCryst Structure-Guided Design Expertise



Robust drug
screening
systems



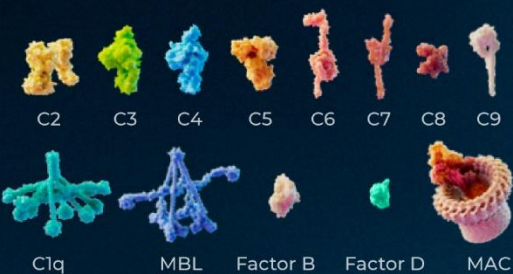
PDB, Cambridge,
& AlphaFold
Protein Structure
Databases



Immersive and
interactive VR
technology

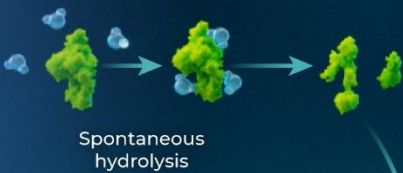
The Complement System

COMPLEMENT PROTEINS



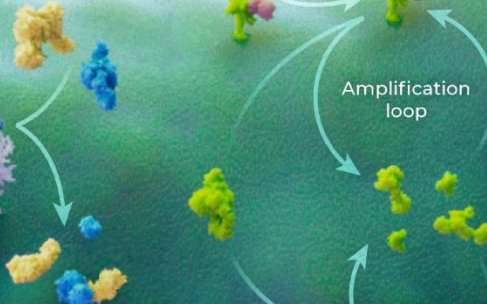
The complement system is part of the innate immune system and is one of the body's first lines of defense against foreign and altered host cells. It is composed of 50+ circulating and membrane-bound proteins.¹⁻³

ALTERNATIVE PATHWAY



LECTIN PATHWAY

Mannose-containing carbohydrate



CLASSICAL PATHWAY

Antigen-bound antibody



Pathogen infection fully activates the complement system

In healthy cells, the complement system triggers a response to non-enveloped viruses

The complement system is involved in apoptotic cell clearance

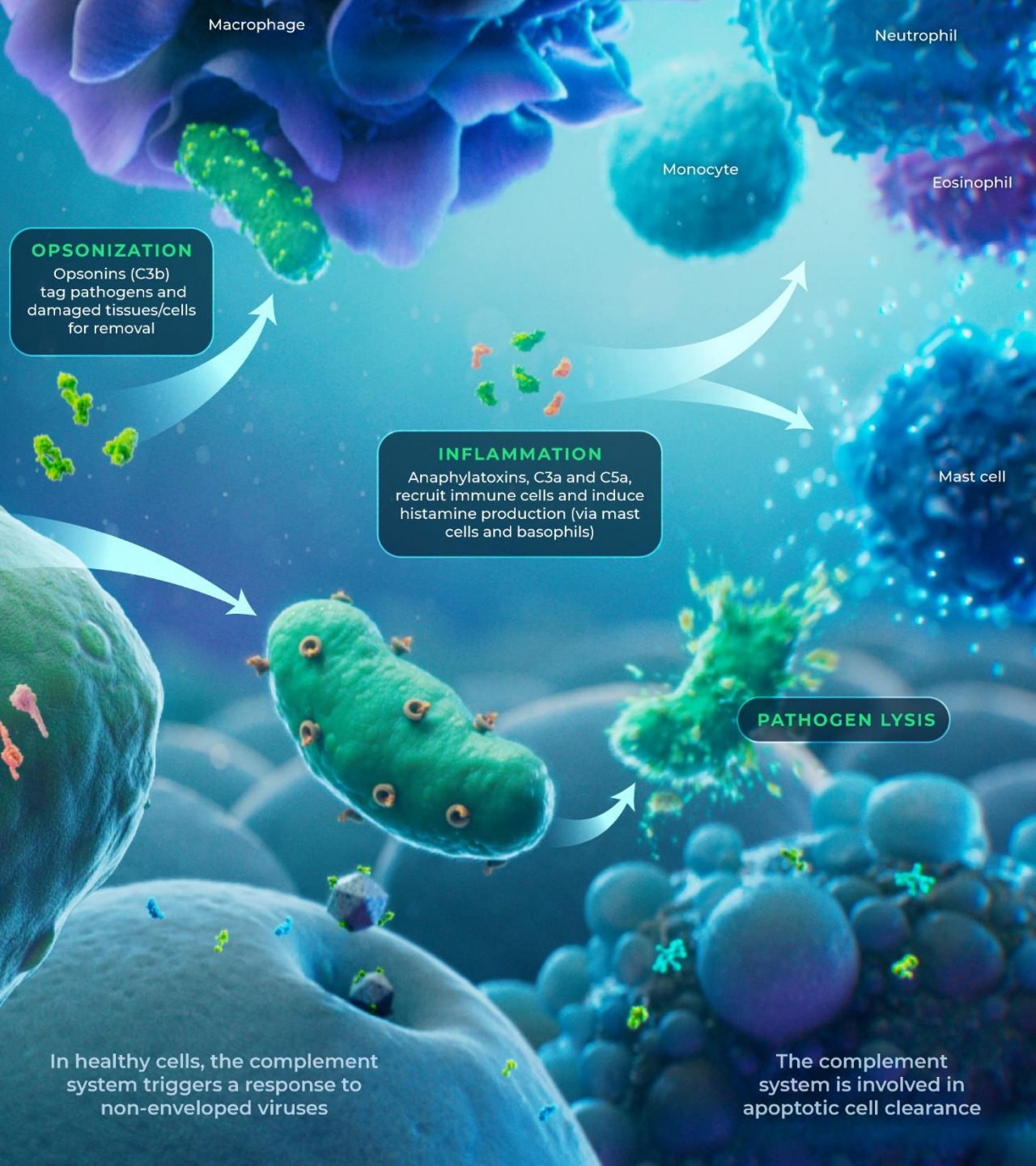
OPSONIZATION

Opsonins (C3b) tag pathogens and damaged tissues/cells for removal

INFLAMMATION

Anaphylatoxins, C3a and C5a, recruit immune cells and induce histamine production (via mast cells and basophils)

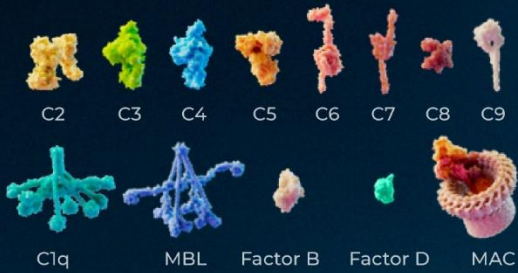
PATHOGEN LYSIS



1. Merle NS, et al. *Front Immunol.* 2015;6:262. 2. Bajic G, et al. *EMBO J.* 2015;34(22):2735-2757. 3. Merle NS, et al. *Front Immunol.* 2015;6:257.

The Complement System

COMPLEMENT PROTEINS



ALTERNATIVE PATHWAY



LECTIN PATHWAY

Mannose-containing carbohydrate



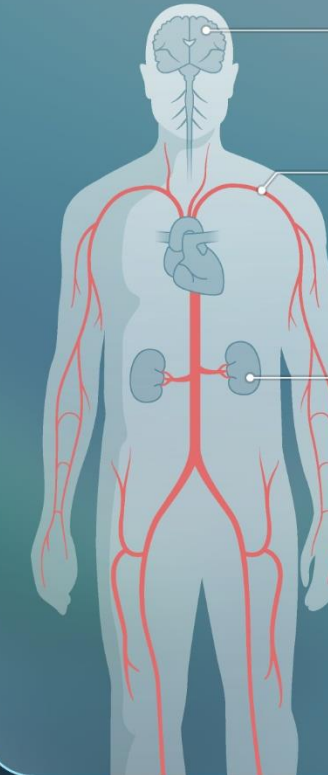
CLASSICAL PATHWAY

Antigen-bound antibody



Amplification loop

Dysregulation can lead to rare neurological, blood, immune, kidney, skin, and other diseases.¹⁻¹¹



NEUROLOGICAL

- Myasthenia gravis
- Neuromyelitis optica

BLOOD & IMMUNE

- PNH
- aHUS
- IgAV
- ANCA-v
- Cold agglutinin disease
- WAHA

KIDNEY

- C3G
- IgAN
- PMN
- LN

SKIN

- Bullous pemphigoid

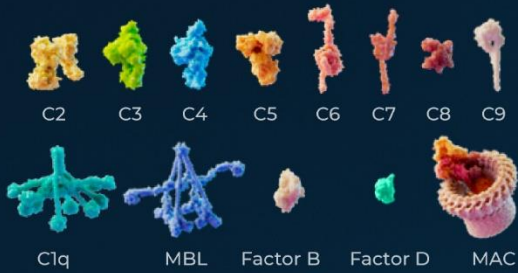
OTHER

- AMD
- anti-GBM

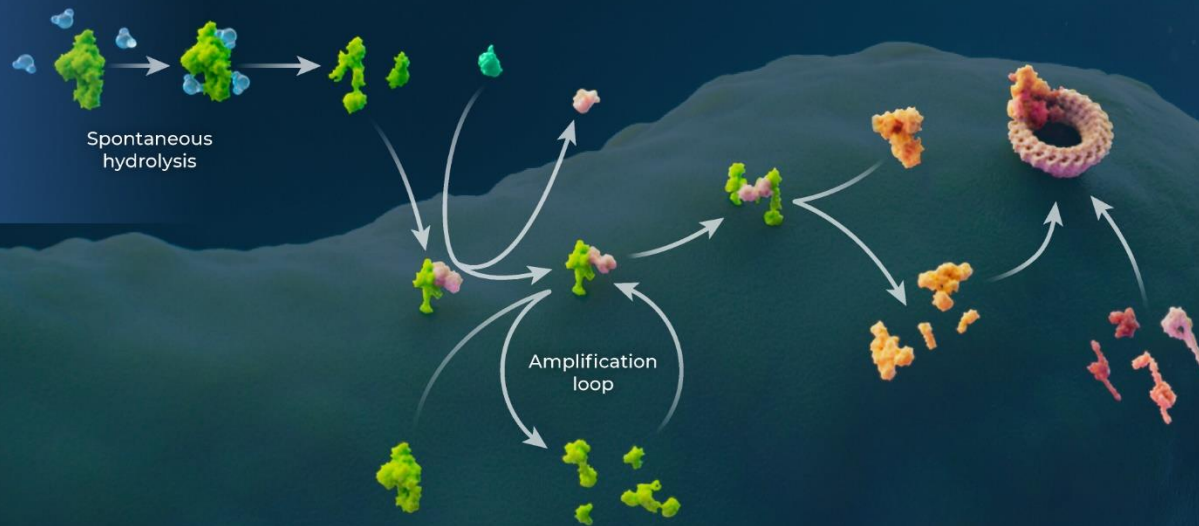
aHUS = atypical hemolytic-uremic syndrome; AMD = age-related macular degeneration; ANCA-v = anti-neutrophil cytoplasmic antibody-associated vasculitis; anti-GBM = anti-glomerular basement membrane; C3G = complement 3 glomerulopathy; IgAN = immunoglobulin A nephropathy; IgAV = immunoglobulin A vasculitis; LN = lupus nephritis; PMN = primary membranous nephropathy; PNH = paroxysmal nocturnal hemoglobinuria; WAHA = warm autoimmune hemolytic anemia.

The Complement System

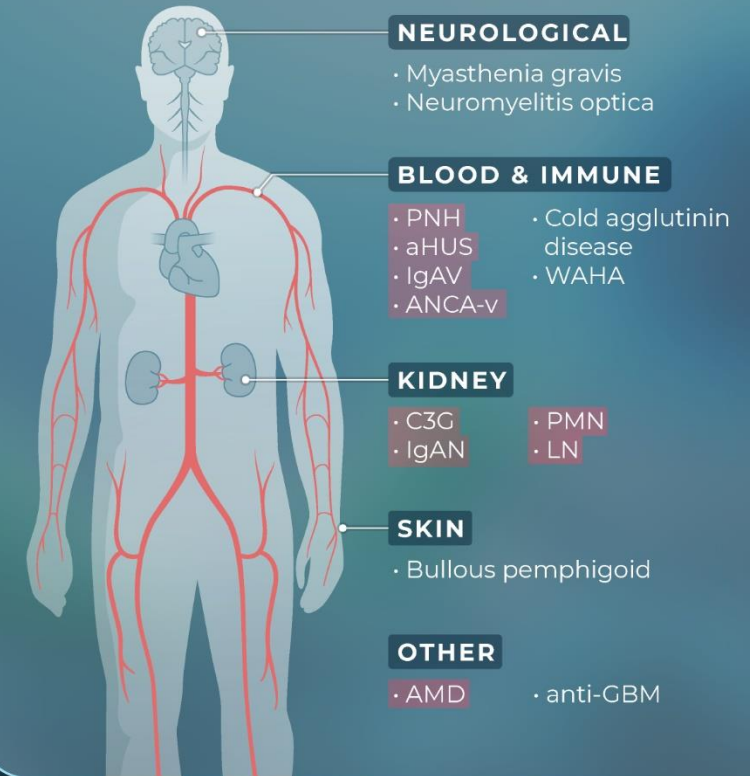
COMPLEMENT PROTEINS



ALTERNATIVE PATHWAY



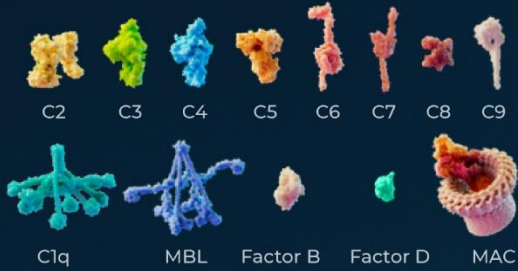
Dysregulation can lead to rare neurological, blood, immune, kidney, skin, and other diseases.¹⁻¹⁵



aHUS = atypical hemolytic-uremic syndrome; AMD = age-related macular degeneration; ANCA-v = anti-neutrophil cytoplasmic antibody-associated vasculitis; anti-GBM = anti-glomerular basement membrane; C3G = complement 3 glomerulopathy; IgAN = immunoglobulin A nephropathy; IgAV = immunoglobulin A vasculitis; LN = lupus nephritis; PMN = primary membranous nephropathy; PNH = paroxysmal nocturnal hemoglobinuria; WAHA = warm autoimmune hemolytic anemia.

The Complement System

COMPLEMENT PROTEINS

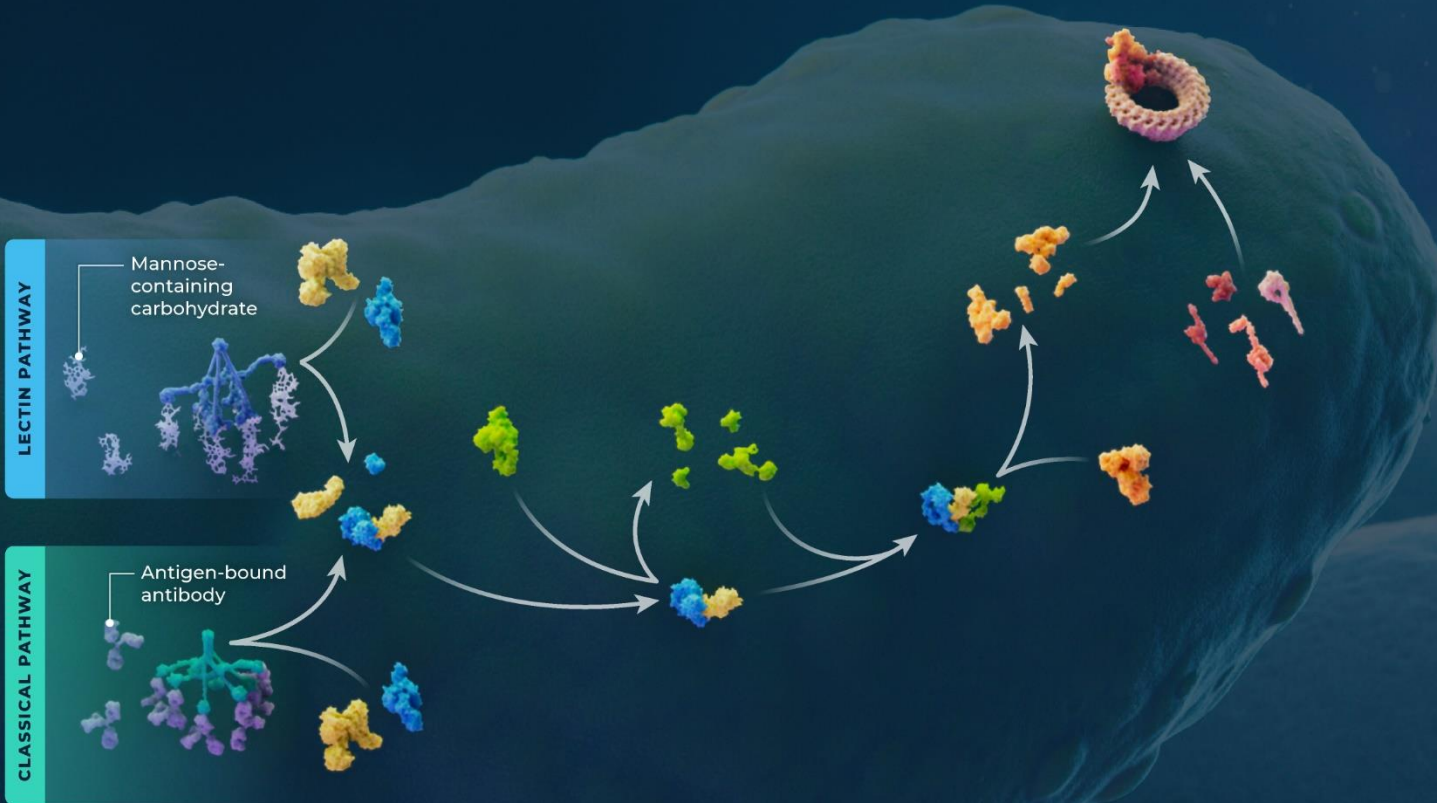


LECTIN PATHWAY

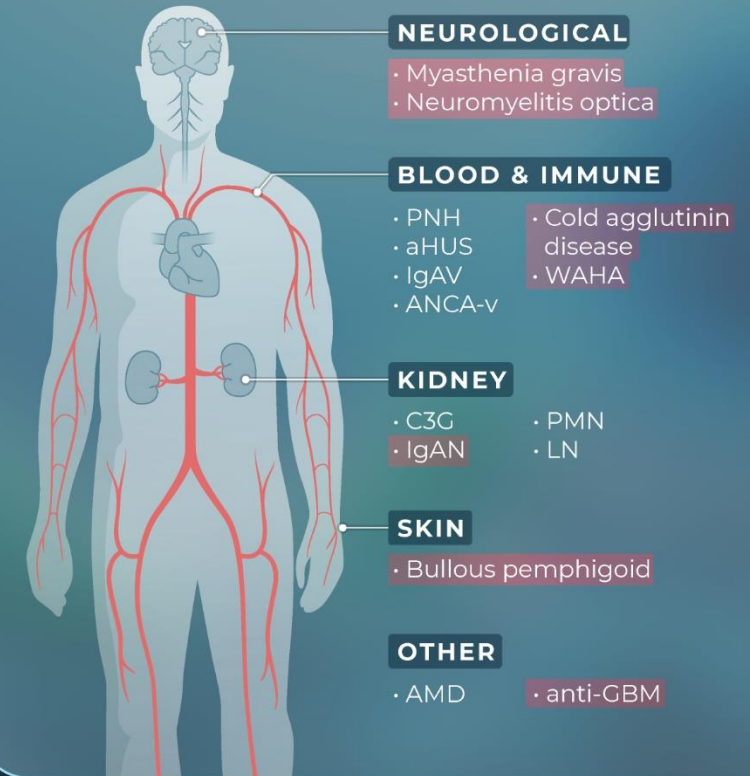
Mannose-containing carbohydrate

CLASSICAL PATHWAY

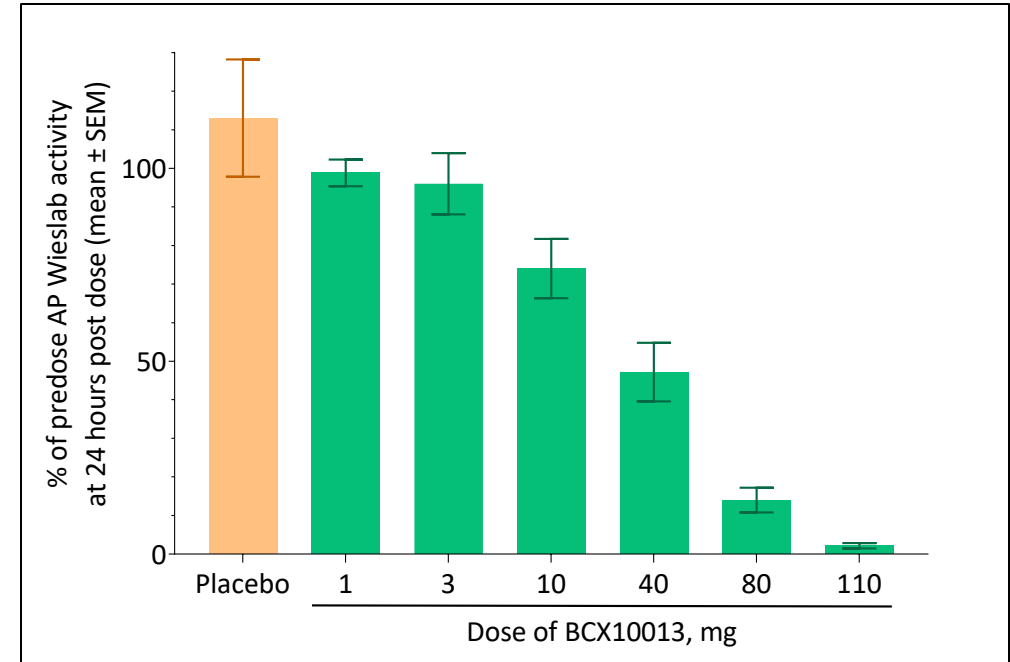
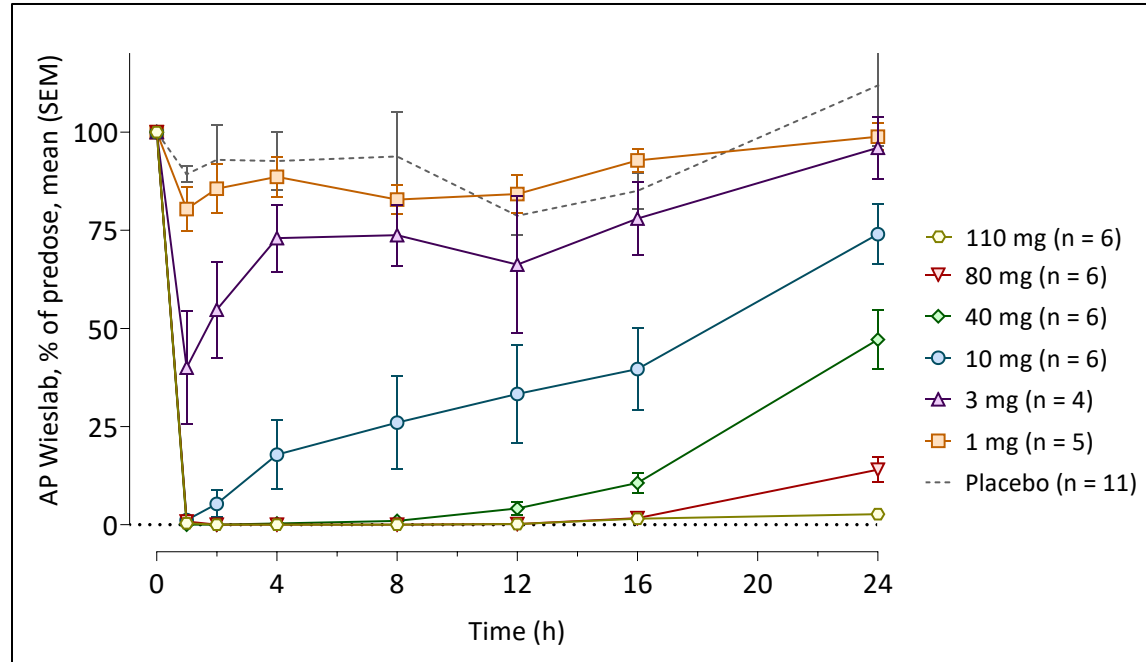
Antigen-bound antibody



Dysregulation can lead to rare neurological, blood, immune, kidney, skin, and other diseases.



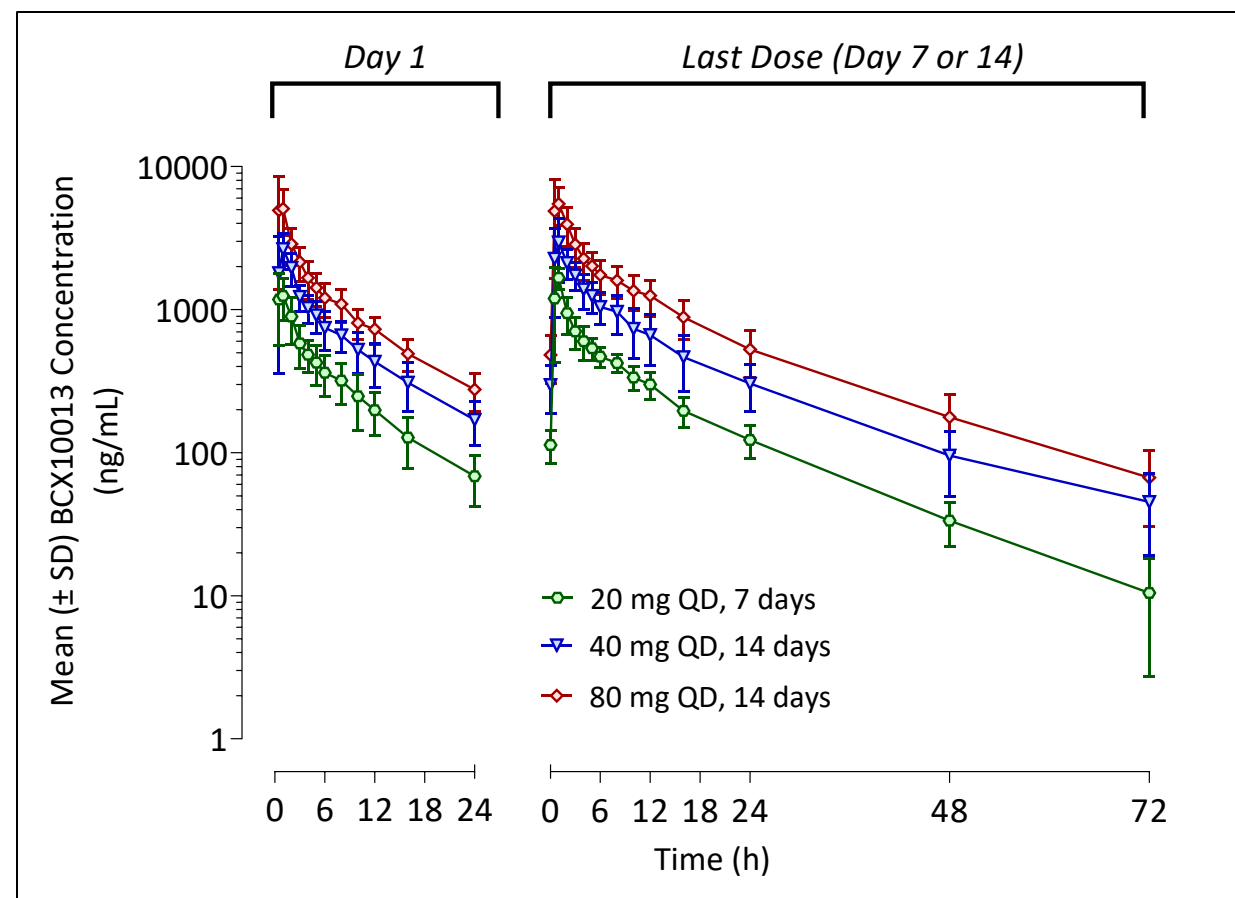
Single doses of BCX10013 resulted in rapid, dose-dependent suppression of alternative pathway of complement



- Suppression of AP activity by BCX10013 was assessed using AP Wieslab assay, which measures functional activity of the complement system
- Following single dose BCX10013 administration, the onset of AP inhibition occurred within 1 hour
- The extent of suppression increased in a dose-dependent manner.
- At the highest single dose level tested to date, 110 mg, AP activity was suppressed by a mean of 97.8% at 24 hours post dose

Pharmacokinetics of BCX10013 oral once-daily administration is characterized by dose proportional exposure and modest accumulation

- Absorption of BCX10013 following oral administration was rapid
- Exposure to BCX10013 was approximately dose proportional over the studied dose range (20 to 80 mg QD)
- Steady state was achieved in 7-14 days of daily dosing, with modest accumulation



BCX10013 Well Tolerated at All Doses To Date

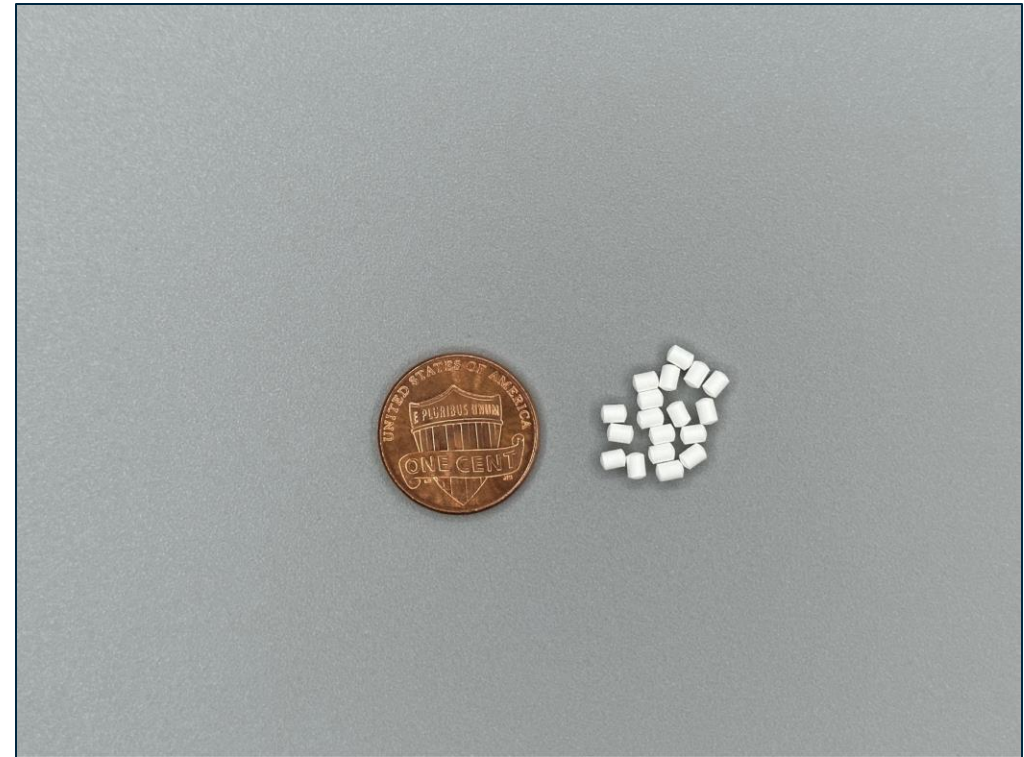
Category of TEAE	All subjects dosed to date (88 active, 20 PBO)	Highest SAD dose			
		110 mg (6 active, 2 PBO)	20 mg QD x 7 days (10 active, 2 PBO)	40 mg QD x 14 days (10 active, 2 PBO)	80 mg QD x 14 days (10 active, 2 PBO)
Any TEAE	43 (40%)	2 (25%)	7 (58%)	7 (58%)	5 (42%)
Serious TEAE	0	0	0	0	0
Any Related TEAE (investigator's assessment to blinded treatment assignment)	4 (4%)	0	0	0	0
Grade 2 TEAE	6 (6%)	0	1 (8%)	1 (8%)	0 (8%)
Grade 3/4 TEAE	0	0	0	0	0
Clinically significant findings in hematology, chemistry, coagulation, urinalysis, vital signs, physical examinations, or ECGs	0	0	0	0	0

Orladeyo Pediatric Trial Enrollment Ongoing

New granule formulation designed to reduce burden of therapy for children with HAE

Trial Details

- Ages 2 to <12
- Enrollment of approximately 20 patients (4 cohorts)
- 12-week standard-of-care therapy, followed by open-label treatment period
- Primary endpoint: Characterization of the PK profile of ORLADEYO in patients aged 2 to <12 years



Debt Refinancing: Better Terms, Longer Maturity, Larger Principal

	New Terms (Pharmakon)	Prior Terms (Athyrium)
Principal Drawn	\$300M	\$200M
Tranches Available (at company option)	\$150M (through September 2024)	None
Rate	3 mo. SOFR + 7.00% With PIK option: +7.25%	3 mo. LIBOR (3.50% cap) + 8.25% With PIK option: +10.25%
Maturity	April 2028	December 2025
Financial Covenants	None	Minimum liquidity \$15M
PIK option	50% of interest for first 6 quarters	Ended Q4 2022

- Puts company on strong financial footing to drive ORLADEYO® revenue toward \$1B peak
- Bullet payment moved to 2028
- Pro forma net cash increased \$26M after repayment of Athyrium debt
- Dramatically reduces company's dependence on capital markets

Finance Summary

(figures in millions)

Q2 2023 Cash Position

Cash, cash equivalents, restricted cash & investments at December 31, 2022	\$444
Cash, cash equivalents, restricted cash & investments at June 30, 2023	\$416
Senior credit facility ^A	\$304

2023 FY Guidance

ORLADEYO [®] revenue	≥\$320
Operating expenses (excluding non-cash comp)	\$375

A – From Pharmakon Advisors, financing of \$450M (\$300M drawn at issuance) with PIK option for 50% of interest for first six quarters; \$3.8M in interest payment-in-kind added to principal since issuance through June 30, 2023; \$150M remaining available to draw at company's option through September 2024



Save the Date:

BioCryst Pharmaceuticals R&D Day

November 3, 2023