J.P. MORGAN HEALTHCARE CONFERENCE

JON STONEHOUSE
PRESIDENT AND CHIEF EXECUTIVE OFFICER

JANUARY 2023

Forward-Looking Statements

BioCryst's presentation may contain forward-looking statements, including statements regarding future results, unaudited and forward-looking financial information and company performance or achievements. These statements are subject to known and unknown risks and uncertainties which may cause our actual results, performance or achievements to be materially different from any future results or performances expressed or implied in this presentation. 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

ORLADEYO: The First and Only Once-daily Oral Prophylactic Therapy for HAE

In hereditary angioedema (HAE),

this is big.

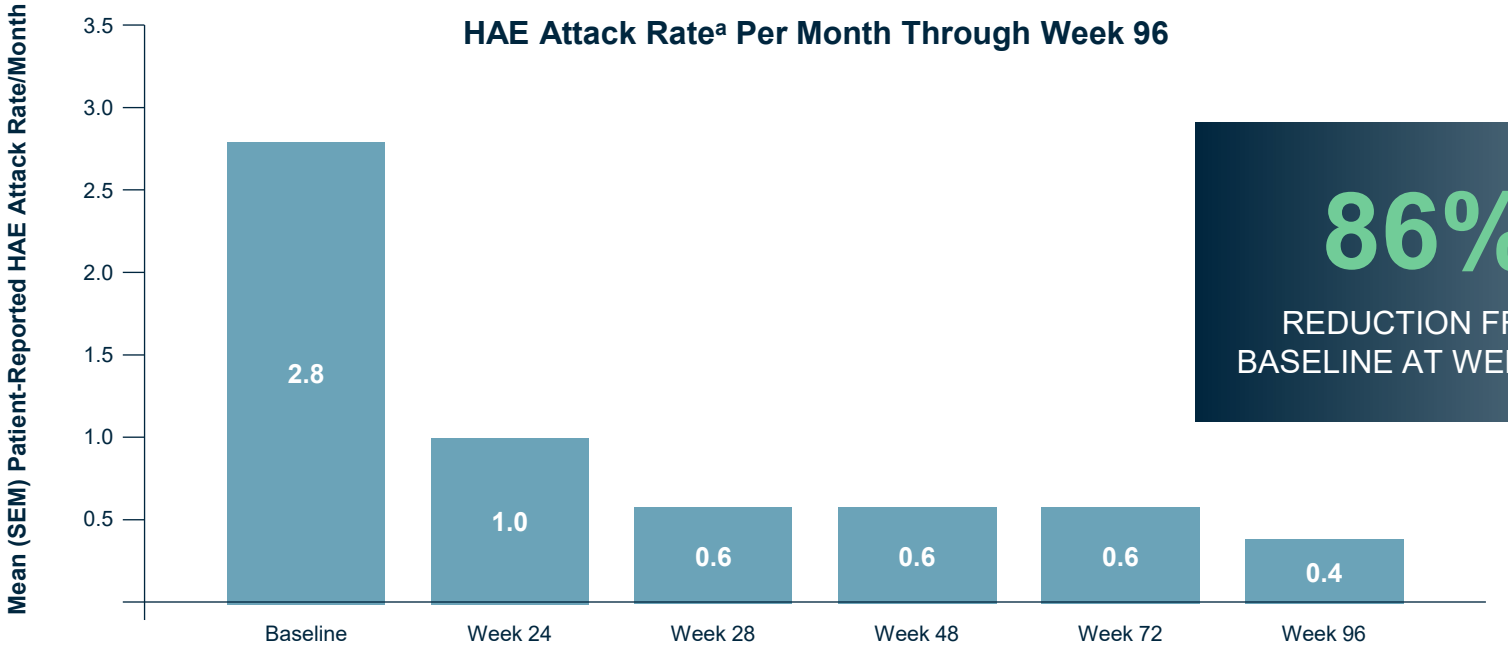
In your day,

this is small.

ORLADEYO® (berotralstat) PROVIDES SUSTAINED ATTACK RATE REDUCTION[1]

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]



86%
REDUCTION FROM BASELINE AT WEEK 96[b,c]

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

SEM, standard error of mean.
[a]Due 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]

[b]This reflects an ad hoc analysis of interim data.[1,2]

[c]86% 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.

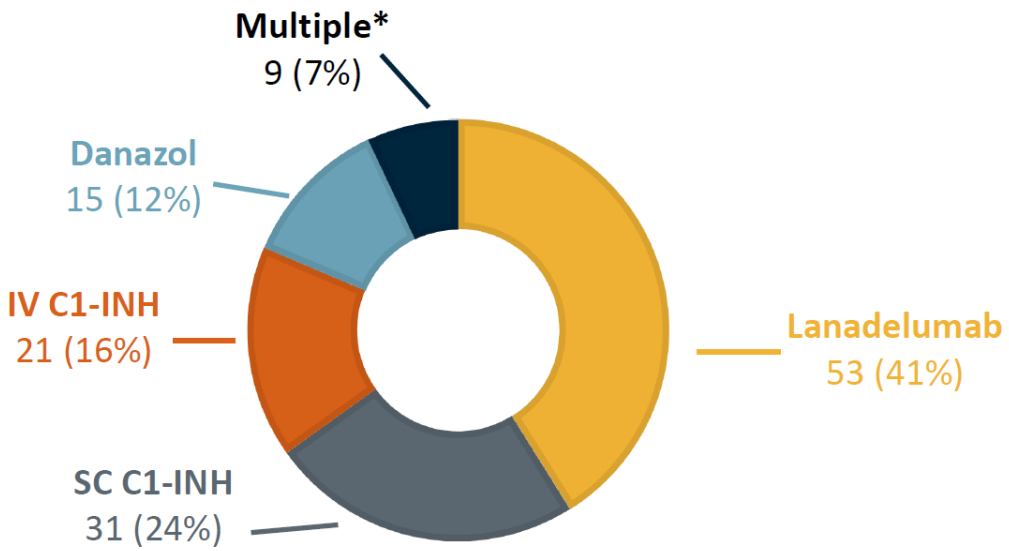
2. Data on file, BioCryst Pharmaceuticals, Inc.

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.

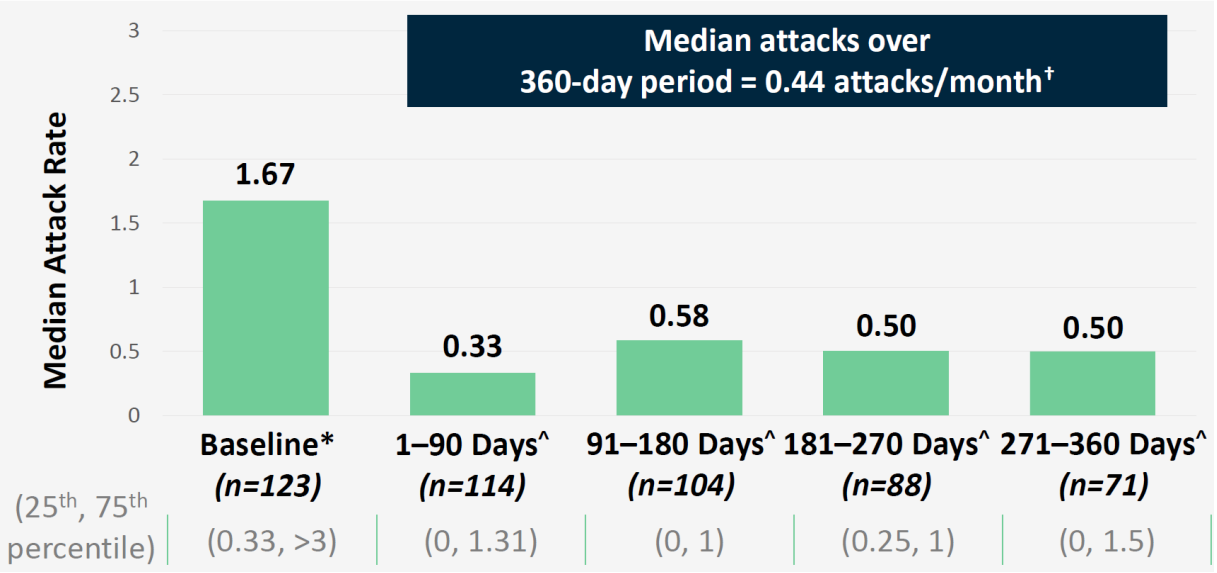
Please see Important Safety Information.

ACAAI: ORLADEYO Real-World Data Show Sustained Reduction in Attacks, Regardless of Prior Therapy[1]

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

1. Marc A. Riedl et al. Presented at: American College of Allergy Asthma and Immunology Annual Scientific Meeting; November 10-14, 2022.

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)

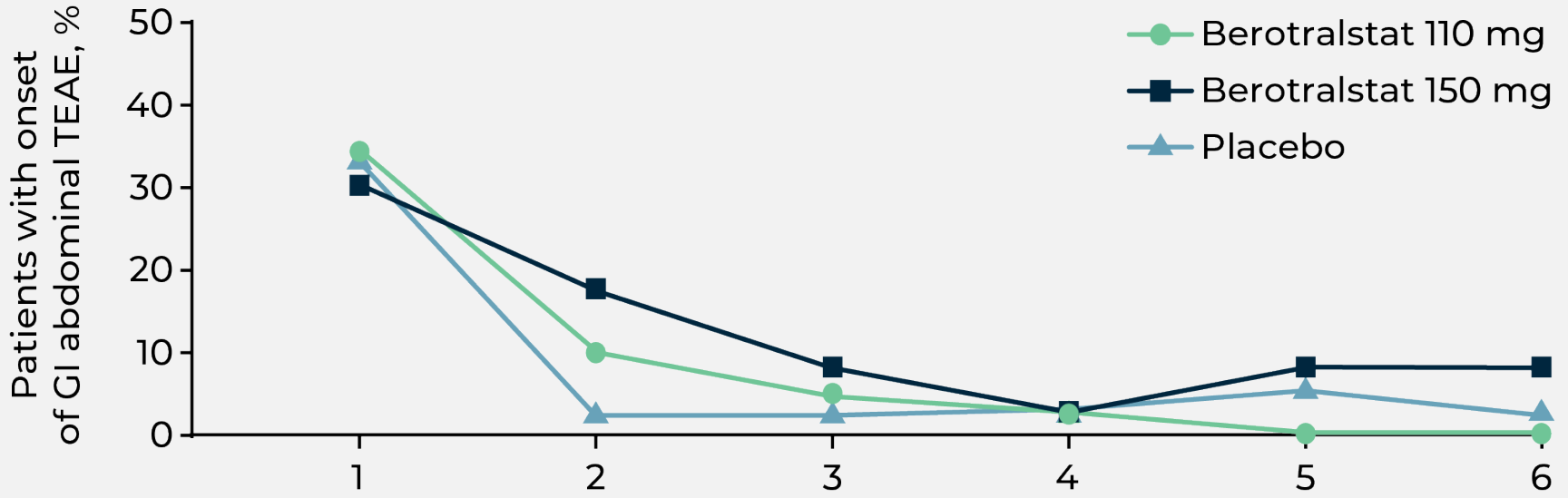
Adverse reactions	Placebo (n=39)	ORLADEYO 110 mg (n=41)	ORLADEYO 150 mg (n=40)
	n (%)	n (%)	n (%)
Abdominal pain[b]	4 (10)	4 (10)	9 (23)
Vomiting	1 (3)	4 (10)	6 (15)
Diarrhea[c]	0	4 (10)	6 (15)
Back pain	1 (3)	1 (2)	4 (10)
GERD	0	4 (10)	2 (5)

[a]≥10% and higher than placebo. [b]Includes abdominal pain, abdominal discomfort, abdominal tenderness, and upper abdominal pain. [c]Includes 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



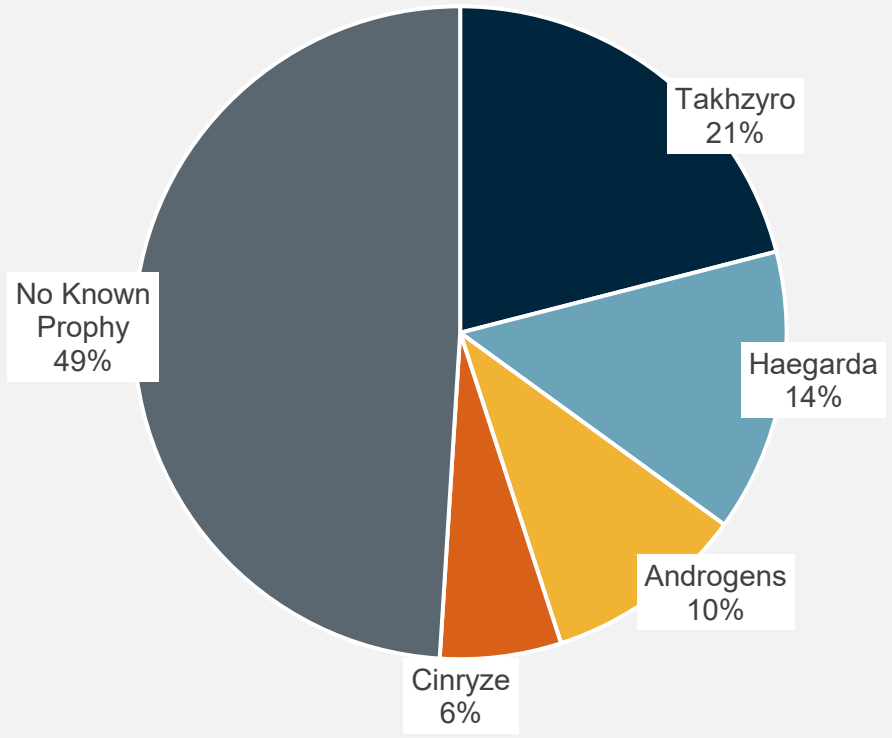
Patients on study drug:						
Berotralstat 110 mg	41	41	41	41	40	38
Berotralstat 150 mg	40	40	37	37	37	37
Placebo	39	39	38	37	36	34

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

Patient + Prescriber Trends Support Continued Growth

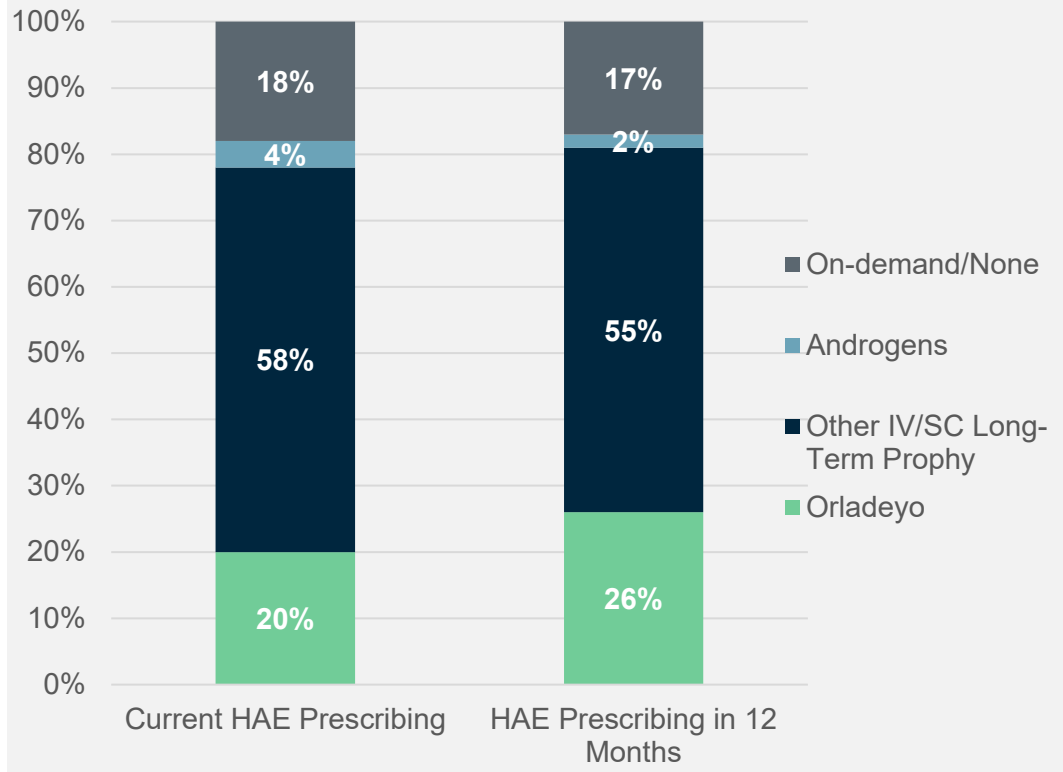
7,500 diagnosed & treated HAE pts in U.S.
Established U.S. switch market currently @ 70% prophy/30% acute

Previous HAE Medication



Source: Estimates from internal analysis of consented, non-clinical ORLADEYO patients starting therapy Dec'20-Oct'22

Current and Future Prescribing of Prophy Medication: Mean % of Patients



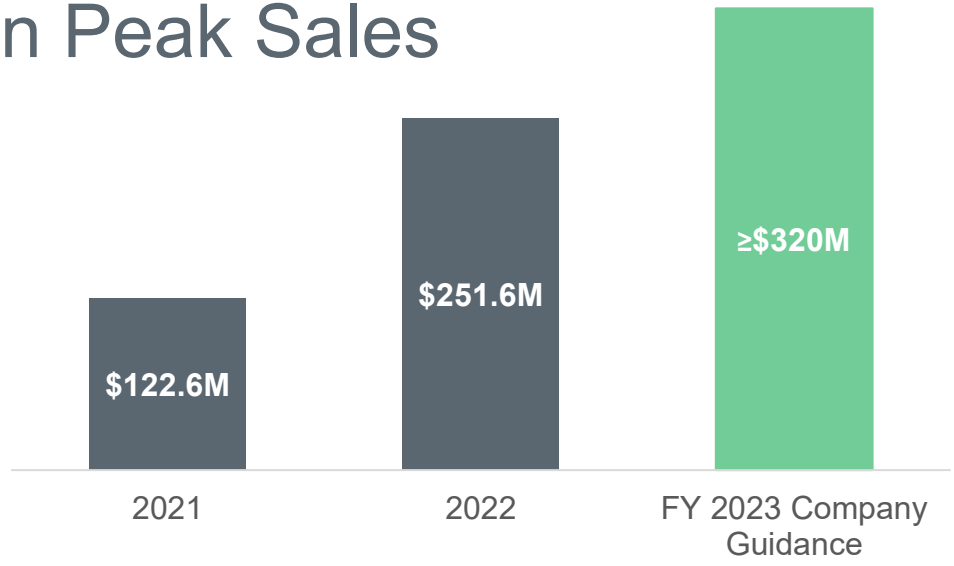
Source: BioCryst proprietary market research survey conducted with 60 Allergist/ Immunologists in Sep'22

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

Our Goal: Be the Accurate Source of Guidance

- With a sole-source specialty pharmacy model in the U.S., BioCryst has complete and real-time access to ORLADEYO Rx data.

- Full year guidance for 2023: ≥$320M

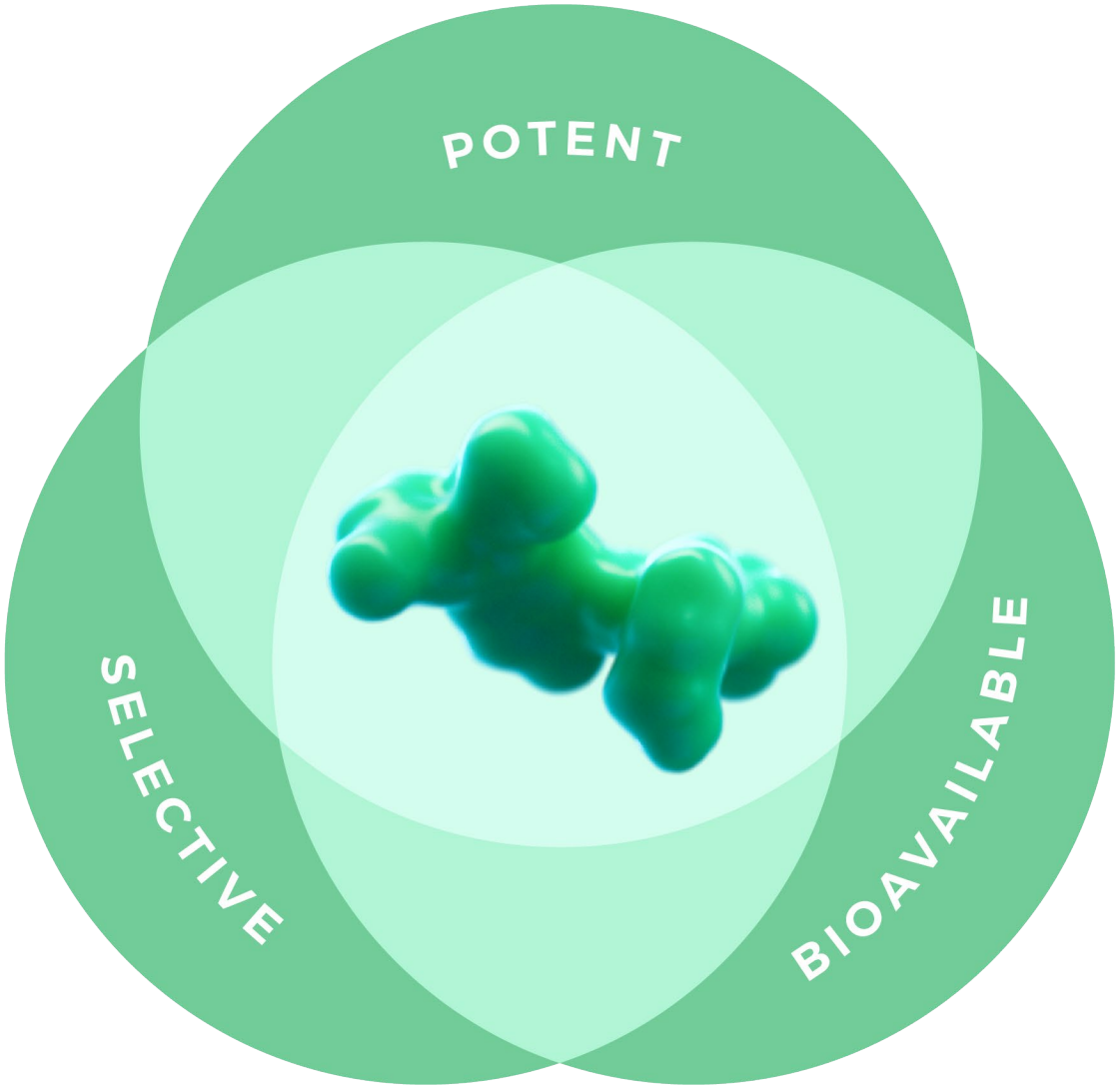
Track Record of Accuracy Since Launch:

(in millions)	2021	2022
Initial BCRX Guidance	≥$100	≥$250
Intra-year updated BCRX guidance	$115-$120	$255-$265
Final guidance provided	$115-$120	$255
Actual FY Revenue	$122.6	$251.6

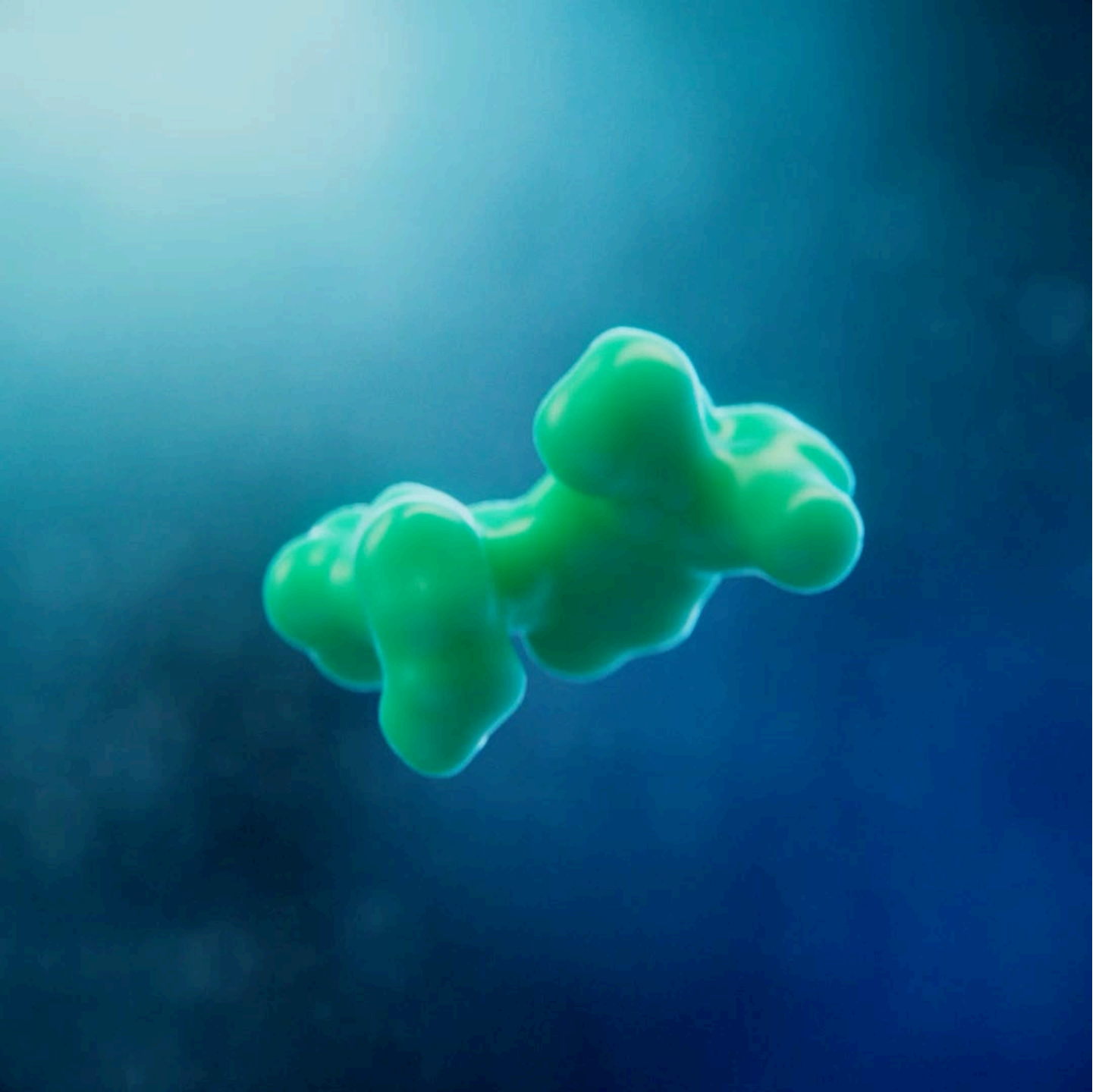
What’s next?

Why is it so hard to design drugs that inhibit complex enzymes, such as serine proteases?

An effective drug must be **potent**, **selective**, and **bioavailable** – 3 critical characteristics.



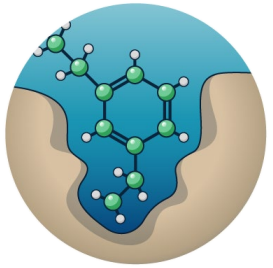
Turk B. *Nat Rev Drug Discov.* 2006;5(9):785-799.



Properties Affecting Potency[1-3]

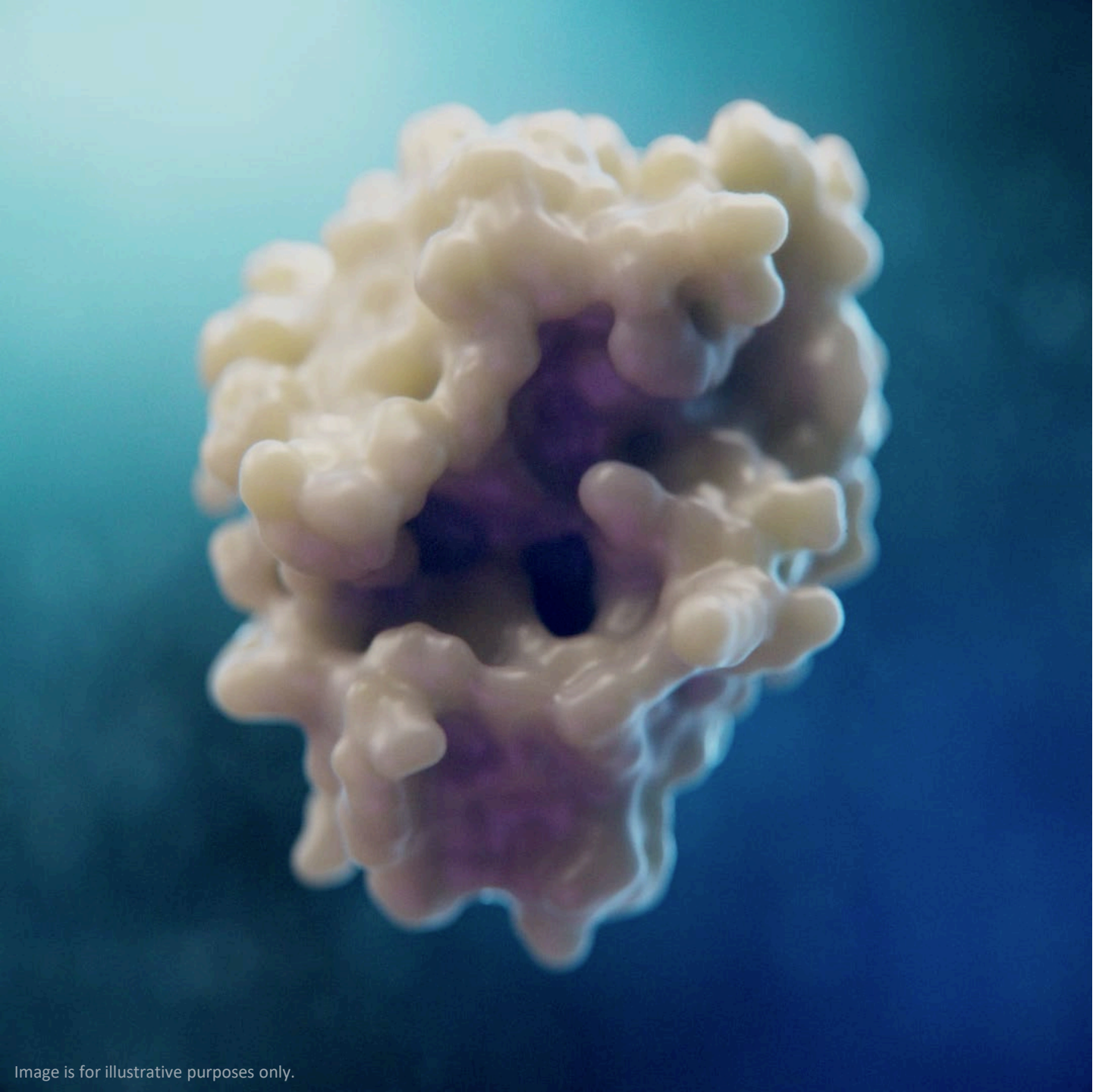
Physical shape

Electrostatic properties



Specific atoms

1. Turk B. *Nat Rev Drug Discov*. 2006;5(9):785-799. 2. Currie GM. *J Nucl Med Technol*. 2018;46(2):81-86.
3. Batool M, et al. *Int J Mol Sci*. 2019;20(11):2783.



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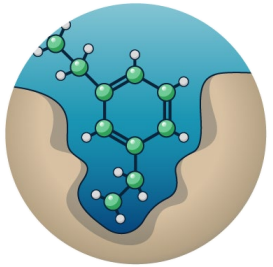

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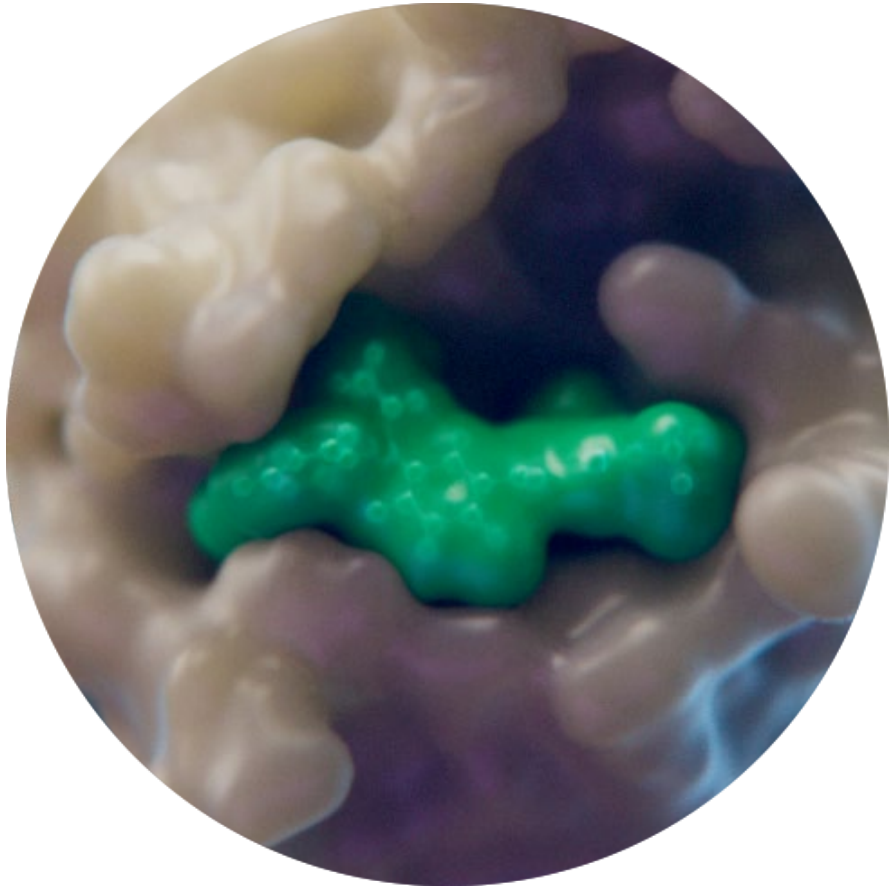
3. Batool M, et al. *Int J Mol Sci*. 2019;20(11):2783.

Co-crystallization



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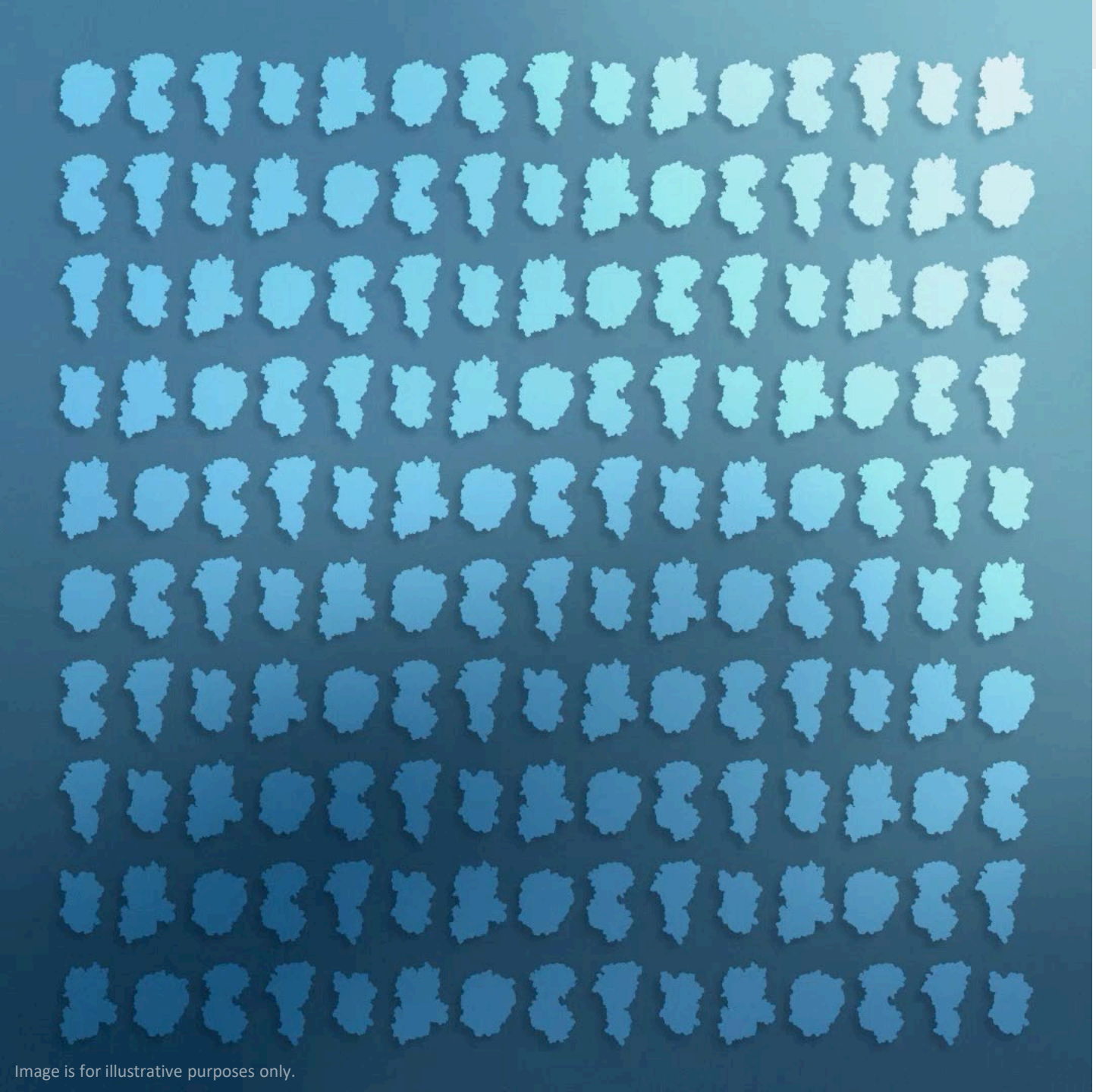

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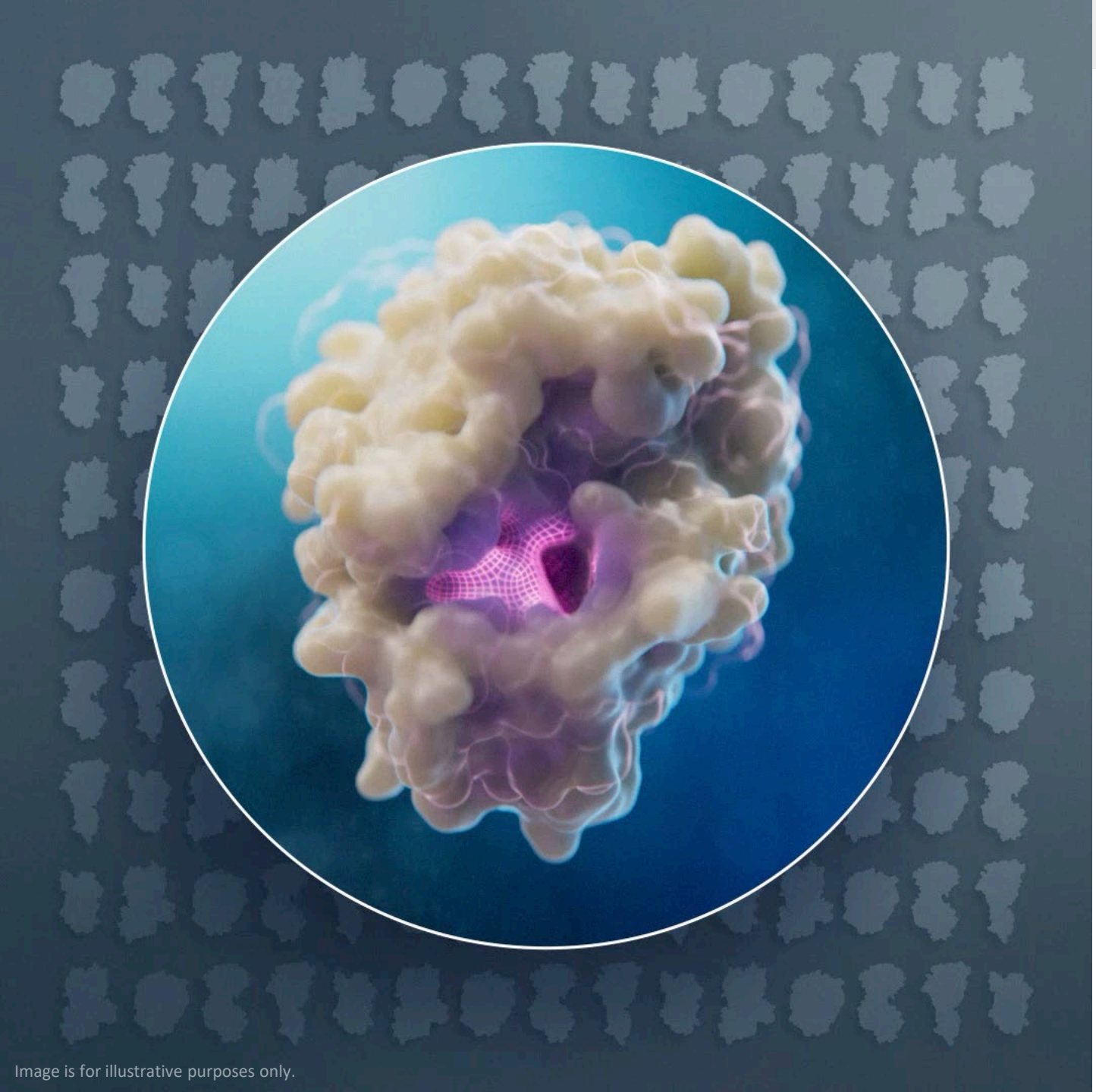
Inhibiting a Specific Serine Protease[1-6]

- 300+ proteases
- **Structure = function:** similar core function of cleaving protein's peptide bonds = overlapping active site features
- Must understand physical and electrostatic properties of closely-related serine proteases to identify unique features to inhibit

1. Di Cera E. *IUBMB Life*. 2009;61(5):510-515. 2. Puente XS, et al. *Nat Rev Genet*. 2003;4(7):544-558. 3. Bond JS. *J Biol Chem*. 2019;294(5):1643-1651. 4. Hvidsten TR, et al. *PLoS One*. 2009;4(7):e6266. 5. Turk B. *Nat Rev Drug Discov*. 2006;5(9):785-799. 6. Huggins DJ, et al. *J Med Chem*. 2012;55(4):1424-1444.



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- 300+ proteases
- **Structure = function:** similar core function of cleaving protein's peptide bonds = overlapping active site features
- Must understand physical and electrostatic properties of closely-related serine proteases to identify unique features to inhibit
- BioCryst has robust databases and 30+ years of expertise on intimate structural details of serine and other proteases

1. Di Cera E. *IUBMB Life*. 2009;61(5):510-515. 2. Puente XS, et al. *Nat Rev Genet*. 2003;4(7):544-558. 3. Bond JS. *J Biol Chem*. 2019;294(5):1643-1651. 4. Hvidsten TR, et al. *PLoS One*. 2009;4(7):e6266. 5. Turk B. *Nat Rev Drug Discov*. 2006;5(9):785-799. 6. Huggins DJ, et al. *J Med Chem*. 2012;55(4):1424-1444.

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Oral Drugs Must Enter the Bloodstream[1,2]

- Competes directly with potency and selectivity
- Must optimize electrostatic charge and molecular weight so that the molecule is soluble and absorbed into the bloodstream

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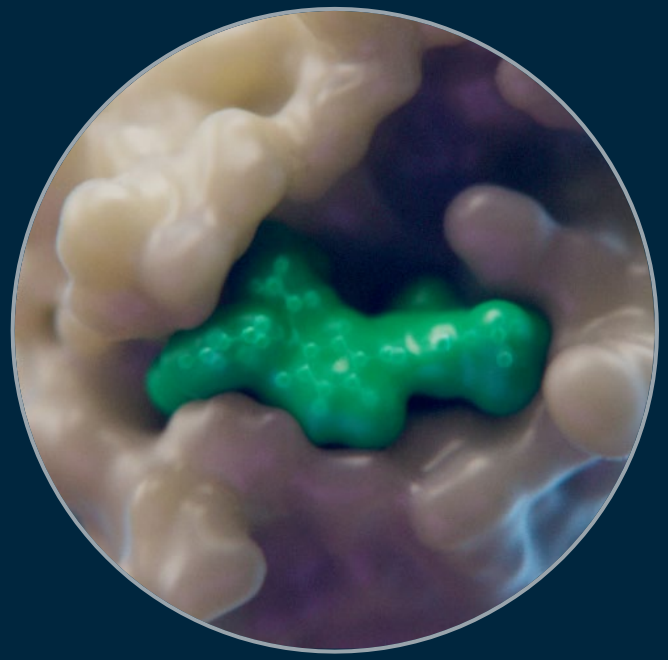
Oral Drugs Must Enter the Bloodstream[1,2]

- Competes directly with potency and selectivity
- Must optimize electrostatic charge and molecular weight so that the molecule is soluble and absorbed into the bloodstream
- BioCryst can modify distinct properties of a molecule to improve bioavailability without sacrificing potency and selectivity

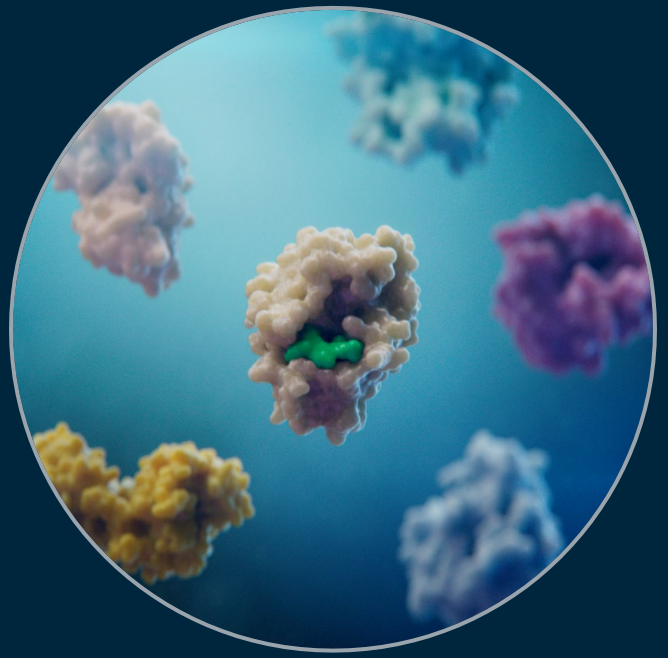
1. Turk B. *Nat Rev Drug Discov*. 2006;5(9):785-799. 2. Gleeson MP, et al. *Nat Rev Drug Discov*. 2011;10(3):197-208.

3 Critical Factors for Successful Drug Design



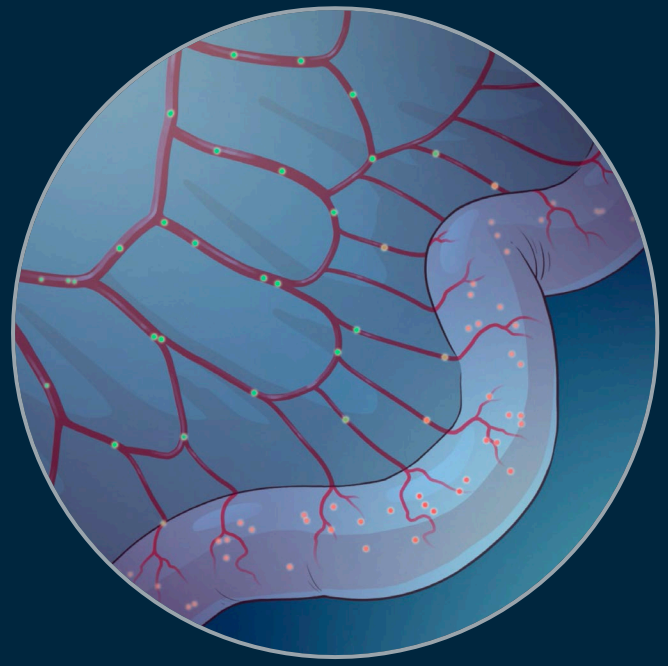
Potency

Needs to bind physically and electrostatically to inhibit an ever-changing target[1-3]



Selectivity

Needs unique, identifiable features that inhibit a specific serine protease[4]

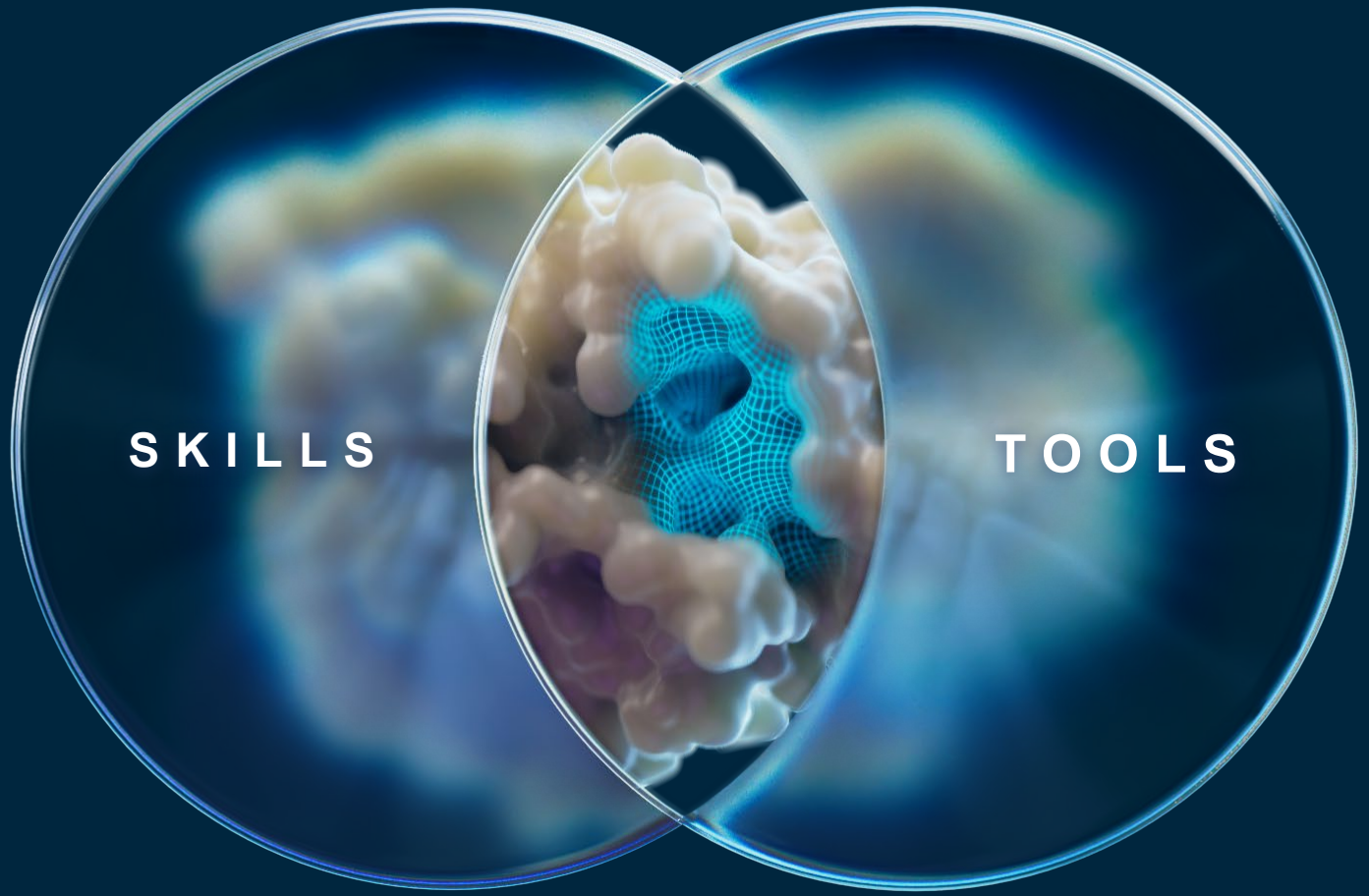


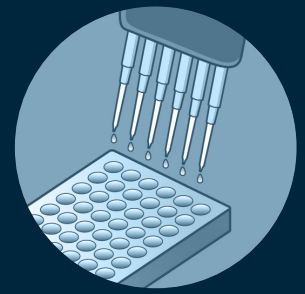
Bioavailability

Oral molecules need to be soluble to cross from the GI tract into the bloodstream[5]

1. Currie GM. *J Nucl Med Technol*. 2018;46(2):81-86. 2. Batool M, et al. *Int J Mol Sci*. 2019;20(11):2783. 3. Turk B. *Nat Rev Drug Discov*. 2006;5(9):785-799. 4. Huggins DJ, et al. *J Med Chem*. 2012;55(4):1424-1444.
5. Alqahtani MS, et al. *Front Pharmacol*. 2021;12:618411.

BioCryst Structure-Guided Design Expertise



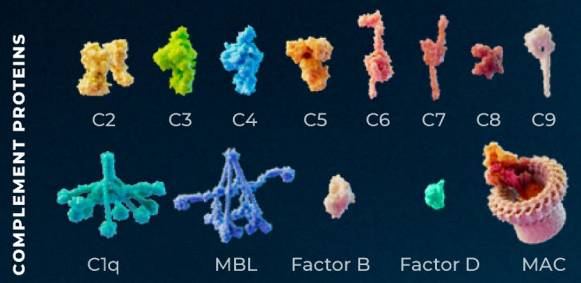


Robust drug screening systems

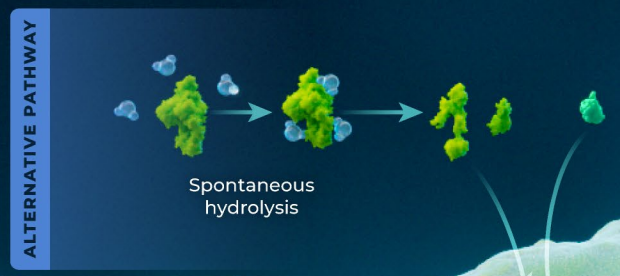
PDB, Cambridge, & AlphaFold Protein Structure Databases

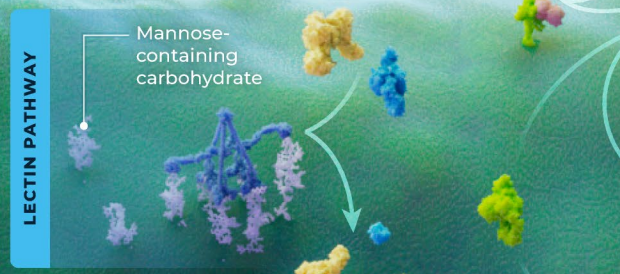
Immersive and interactive VR technology

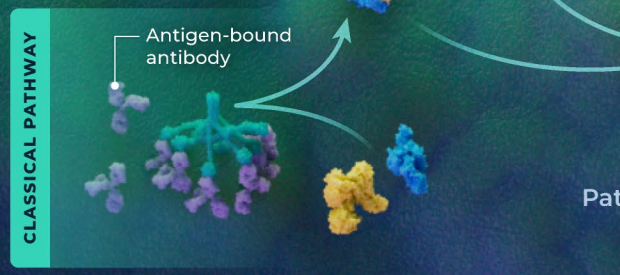
The Complement System



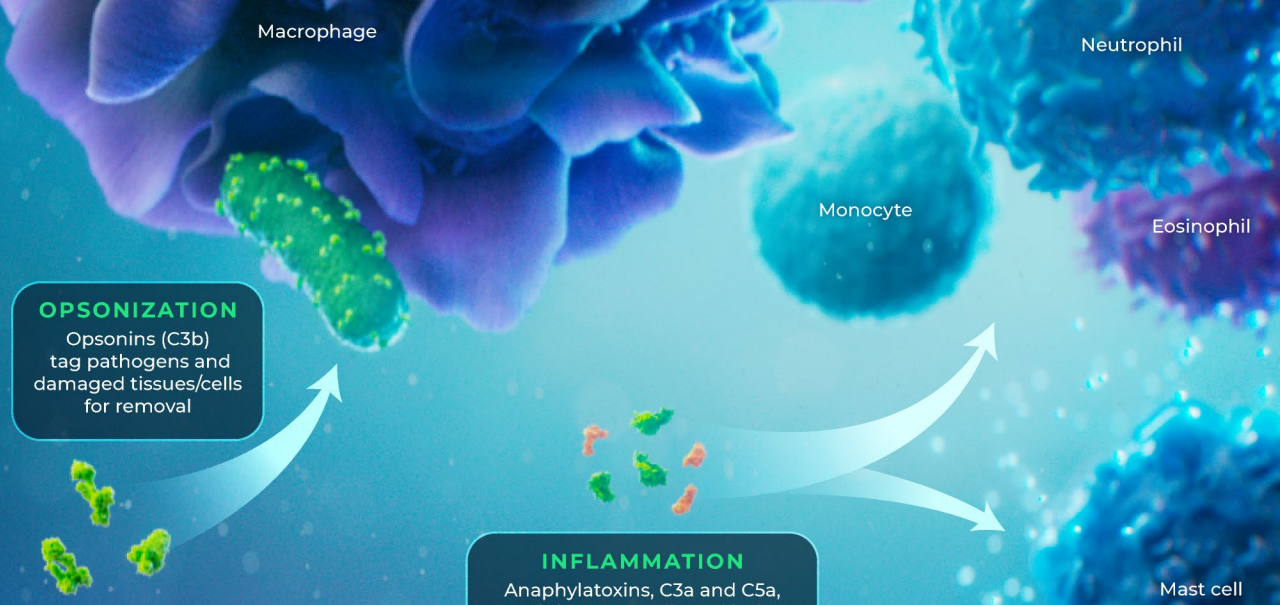
The complement system is part of the innate immune system and is one of the body's first lines of defense against foreign and altered host cells. It is composed of 50+ circulating and membrane-bound proteins.[1-3]

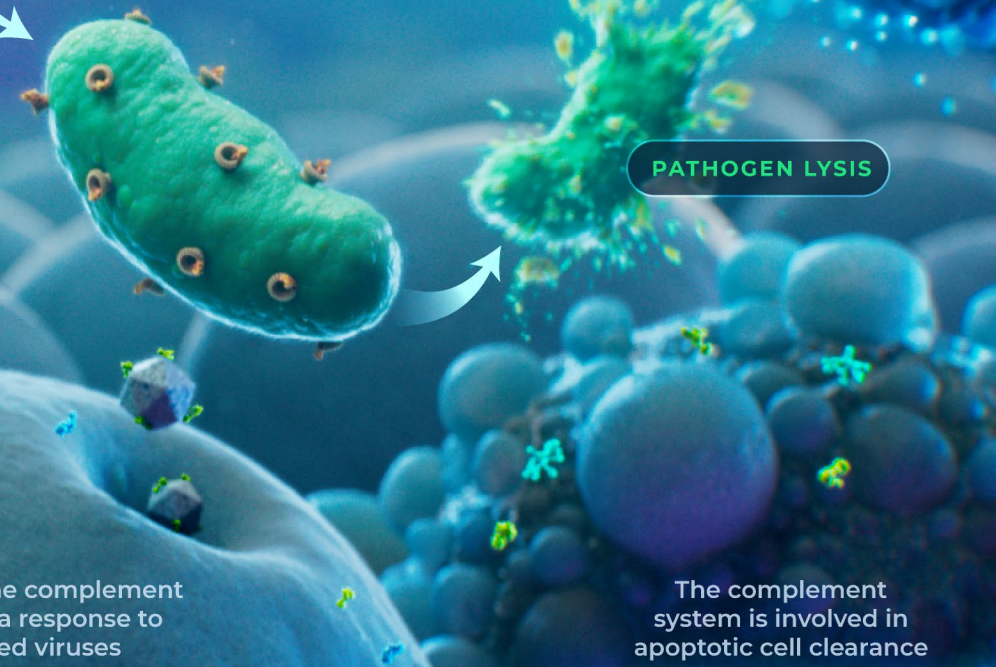






Pathogen infection fully activates the complement system



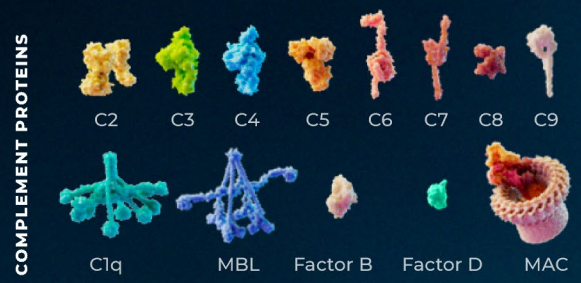


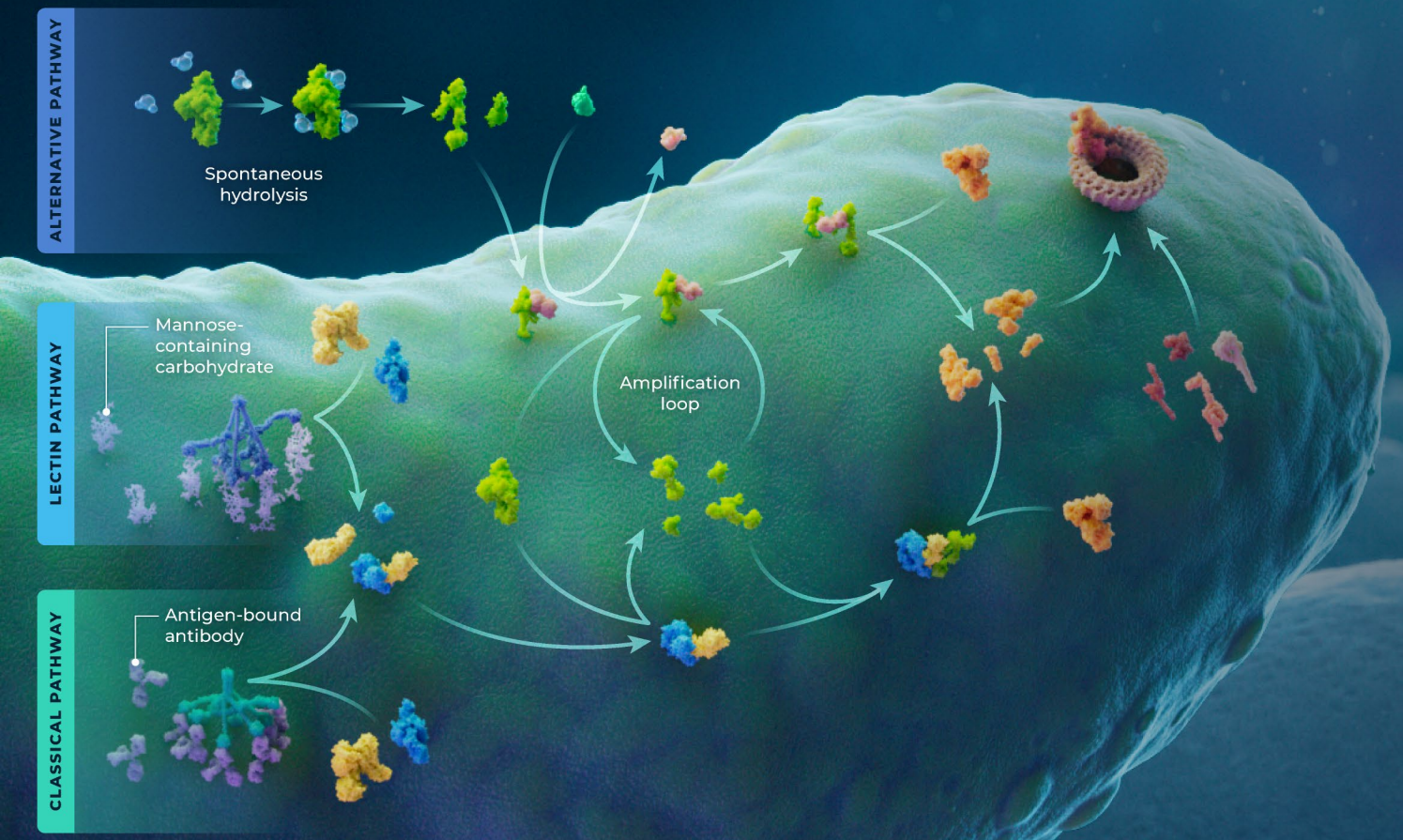
In healthy cells, the complement system triggers a response to non-enveloped viruses

The complement system is involved in apoptotic cell clearance

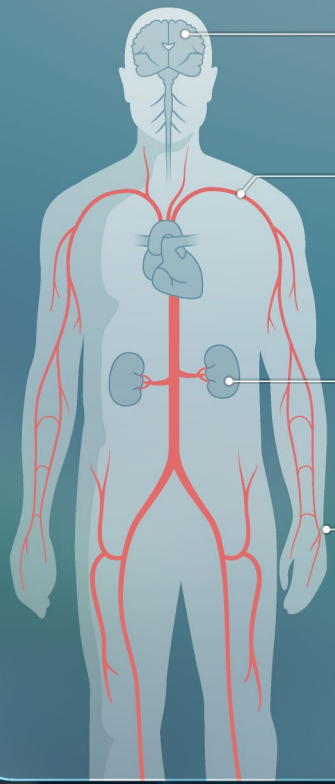
1. Merle NS, et al. *Front Immunol.* 2015;6:262. 2. Bajic G, et al. *EMBO J.* 2015;34(22):2735-2757. 3. Merle NS, et al. *Front Immunol.* 2015;6:257.

The Complement System





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

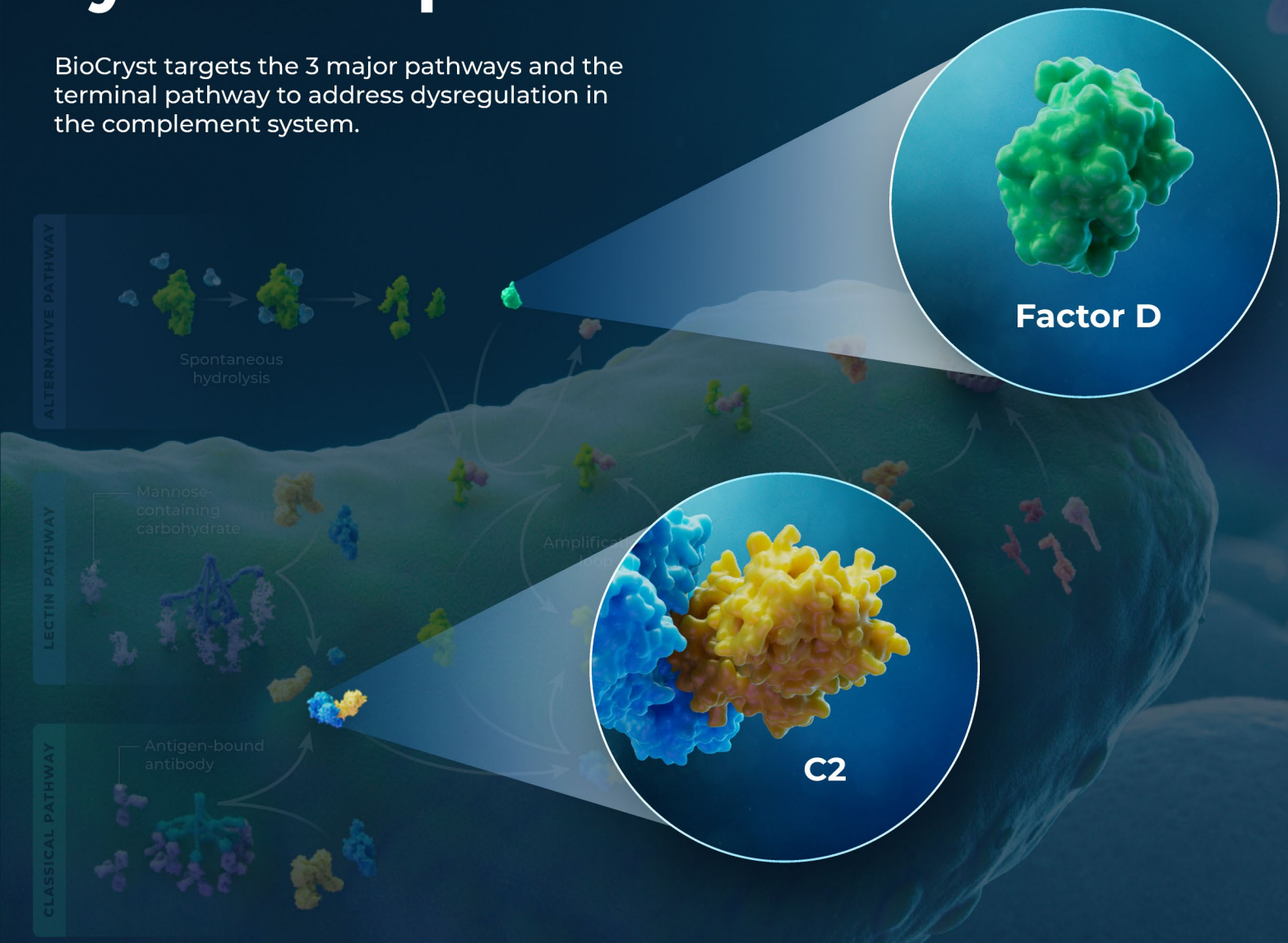
OTHER
- AMD
- anti-GBM

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.

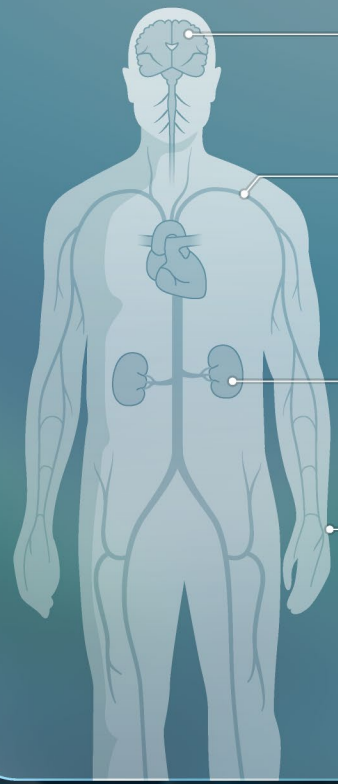
1. Bajic G, et al. *EMBO J*. 2015;34(22):2735-2757. 2. Merle NS, et al. *Front Immunol*. 2015;6:257. 3. Barratt J, et al. *Front Immunol*. 2021;12:712572. 4. Marro J, et al. *Children*. 2022;9:622. 5. Jager U, et al. *Blood*. 2019;133(9):893-901. 6. Berentsen S. *Transfus Med Hemother*.2015;42(5):303-310. 7. Rittner C, et al. *Hum Genet*. 1981;56(3):235-247. 8. So BYF, et al. *Front Immunol*. 2022:13:1009864. 9. Edwards G, et al. *Front Immunol*. 2019;10:1477. 10. Scholl HPN, et al. *PLoS One*. 2008;3(7): e2593. 11. Otten MA, et al. *J Immunol*, 2009, 183: 3980-3988.

BioCryst Complement System Pipeline

BioCryst targets the 3 major pathways and the terminal pathway to address dysregulation in the complement system.



BioCryst is developing novel oral medicines designed to treat rare diseases.



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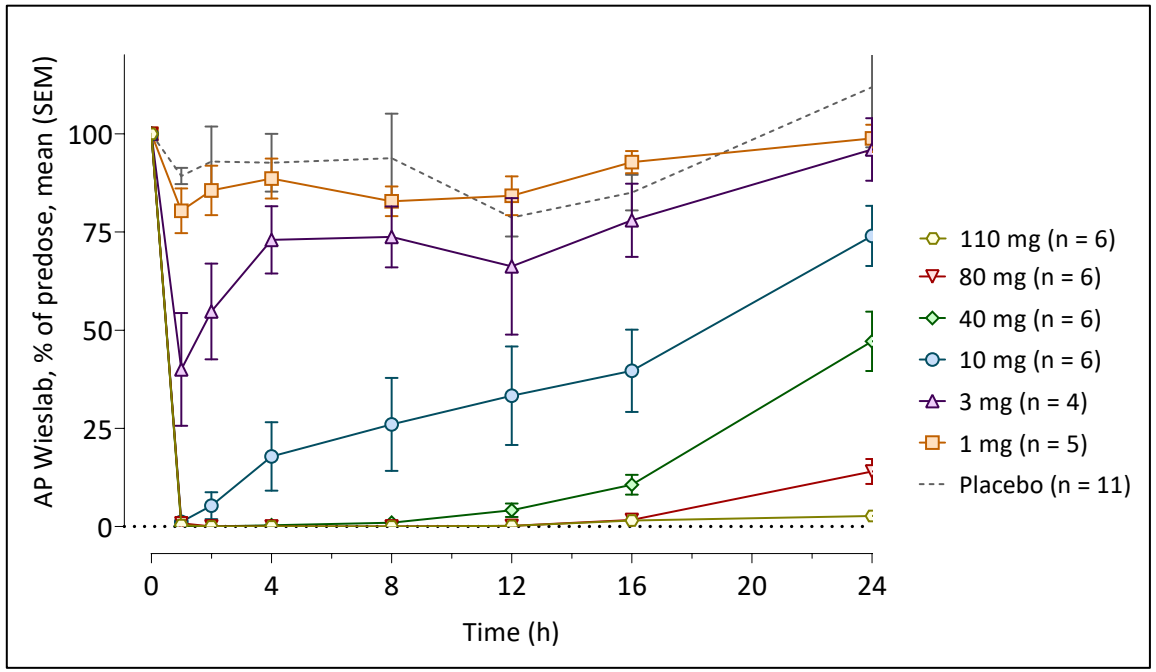
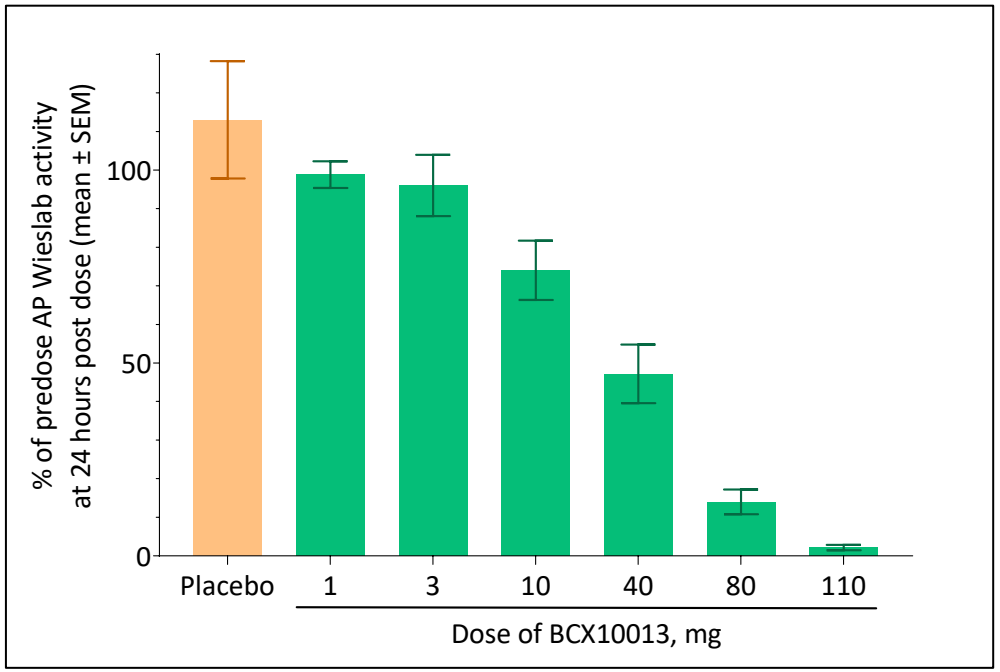
- anti-GBM

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.

POTENTIAL BEST IN CLASS FACTOR D INHIBITOR BCX10013

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

BCX10013 Well Tolerated at All Doses To Date

Category of TEAE	All subjects dosed to date (88 active, 20 PBO)	Highest SAD dose	MAD		
		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%)	1 (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

10013 Development Strategy and Next Steps

Mid-23

Complete SAD/MAD studies and begin patient trials in PNH and renal diseases

YE23

Confirm dose for optimal clinical effect

2024

Begin pivotal study in IgAN (other indications to follow)

Finance Summary

3Q22 Cash Position

Cash, cash equivalents, restricted cash & investments at **September 30, 2021**	**$204M**
Cash, cash equivalents, restricted cash & investments at **September 30, 2022**	**$463M**
Senior Credit Facility[1]	**$232M**

- 2023 R&D expense level expected to be similar to 2022 R&D expense level

- Company plans to provide full operating expense guidance later in Q1 2023

1. From Athyrium Capital Management, term loan of $200M interest-only for 5-year term, $32.4 in interest payment-in-kind (PIK) has been added to principal since issuance

J.P. MORGAN HEALTHCARE CONFERENCE

JON STONEHOUSE
PRESIDENT AND CHIEF EXECUTIVE OFFICER

JANUARY 2023