R&D DAY

BIOCRYST PHARMACEUTICALS

NOVEMBER 3, 2023

FORWARD-LOOKING STATEMENTS

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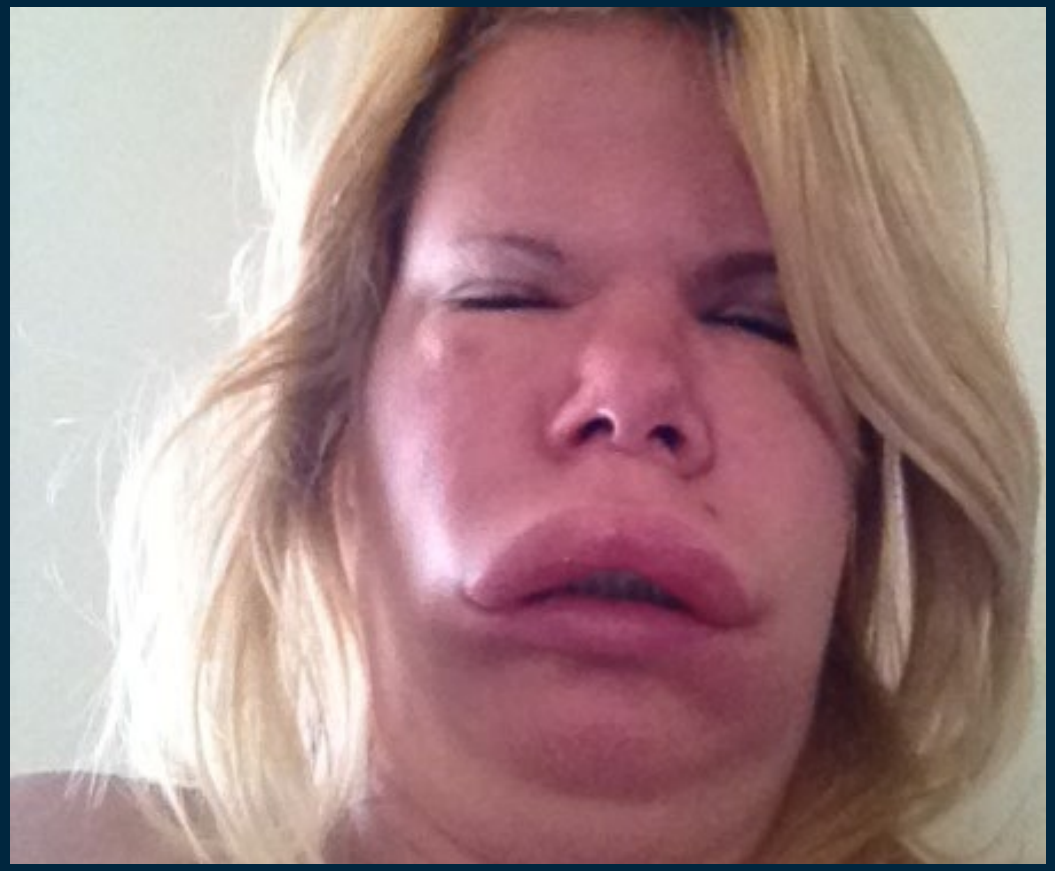
TODAY'S AGENDA

1:00-1:05 (ET)	Welcome	John Bluth, Chief Communications Officer
1:05-1:15	Introduction	Jon Stonehouse, President and Chief Executive Officer
1:15-2:15	BioCryst's Differentiated Approach to R&D	Dr. Helen Thackray, Chief R&D Officer
2:15-3:15	New Molecules and Programs	Charlie Gayer, Chief Commercial Officer Dr. Ryan Arnold, Chief Medical Officer Dr. Bill Sheridan, Chief Development Officer
3:15-3:30	Disciplined Capital Allocation Approach	Anthony Doyle, Chief Financial Officer
3:30 – 4:00	Q&A	

WELCOME

Jon Stonehouse, President & Chief Executive Officer

HELPING RESTORE A SENSE OF FREEDOM FOR PATIENTS WITH HAE



orladeyo®

(berotralstat) capsules 150 mg

OUR BROAD AND DIVERSIFIED 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 in Pediatrics	**Hereditary Angioedema (HAE)**					
BCX10013 Oral Factor D Inhibitor	**Complement-Mediated Diseases**					
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 CP, LP, AP Inhibition	**Complement-Mediated Diseases**					

*Typically Phase 1-2 studies.
†Typically Phase 3 studies.
C5, complement component 5; C2, complement component 2; CP, classical pathway; LP, lectin pathway, AP, alternative pathway.

ADVANCING FUTURE FIRST-IN-CLASS, BEST-IN-CLASS DRUGS FOR PATIENTS WITH RARE DISEASES

Dr. Helen Thackray, Chief Research & Development Officer

DELIVERING BETTER OUTCOMES FOR PATIENTS: FIRST-IN-CLASS, BEST-IN-CLASS THERAPIES FOR RARE DISEASE

- Specialized approach to solve the challenges in drug design
- Focus on first-in-class or best-in-class drugs
- Expanding platform technology producing a diverse pipeline with speed
- Delivering differentiated drugs for better patient outcomes

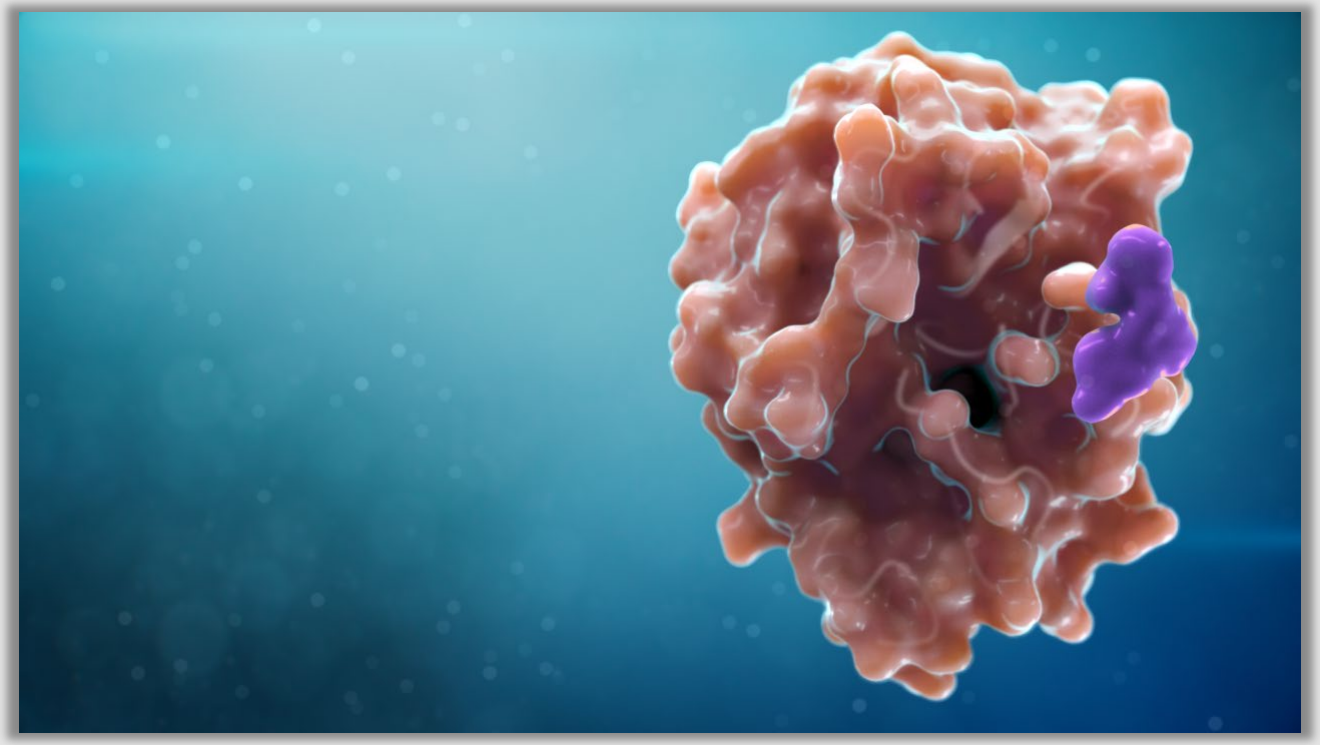
Advancing a broadened pipeline

Plans to deliver proof-of-concept data for
6 molecules in the next 5 years

OVERCOMING THE CHALLENGES OF DEVELOPING A FIRST-IN-CLASS OR BEST-IN-CLASS THERAPY

Designing a Molecule

- High potency
- Target specificity
- Bioavailability



Amino acid sequence

defines how complex 3-D structure folds

To design a differentiated drug

we need to know the final 3-D structure of the protein

PREDICTING THE SHAPE OF AMINO ACIDS STRING IS ONLY A START TO SOLVING FOR COMPLEX DRUG DESIGN

3 Challenges to Overcome

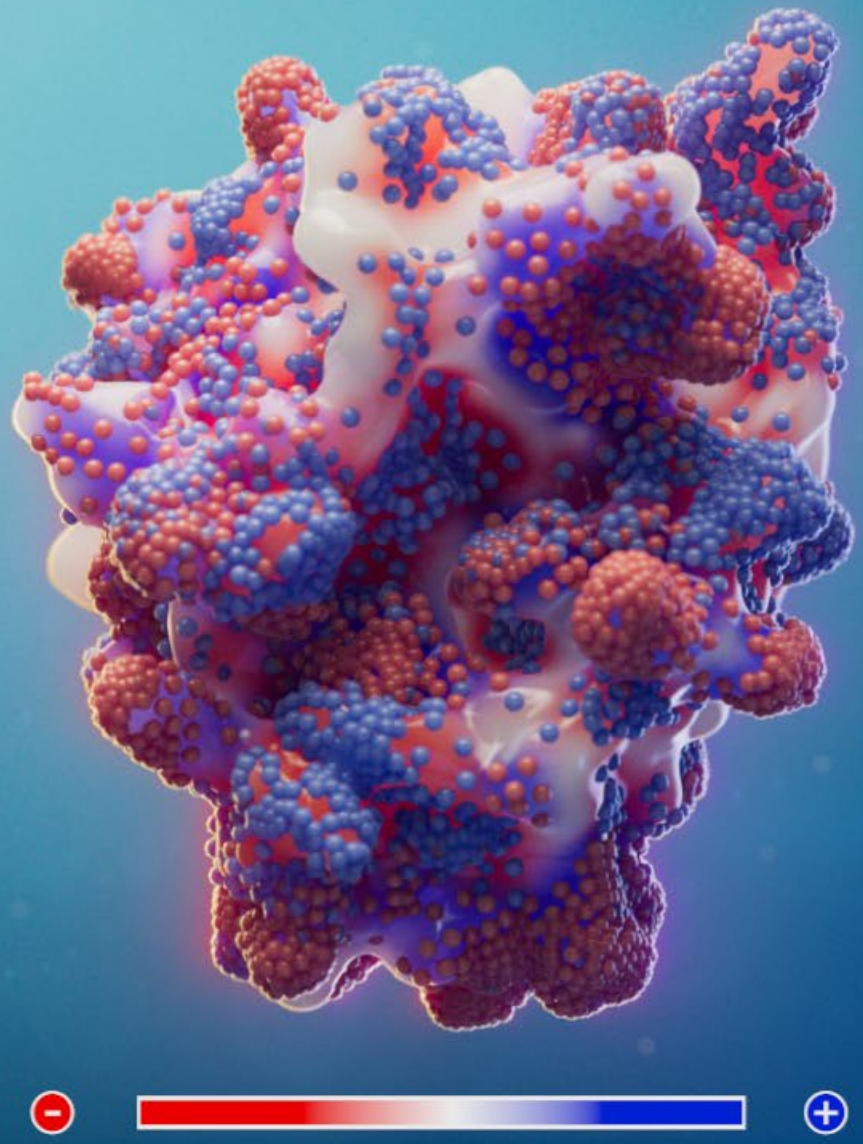
3-dimensional protein structure

High-resolution atomic structure

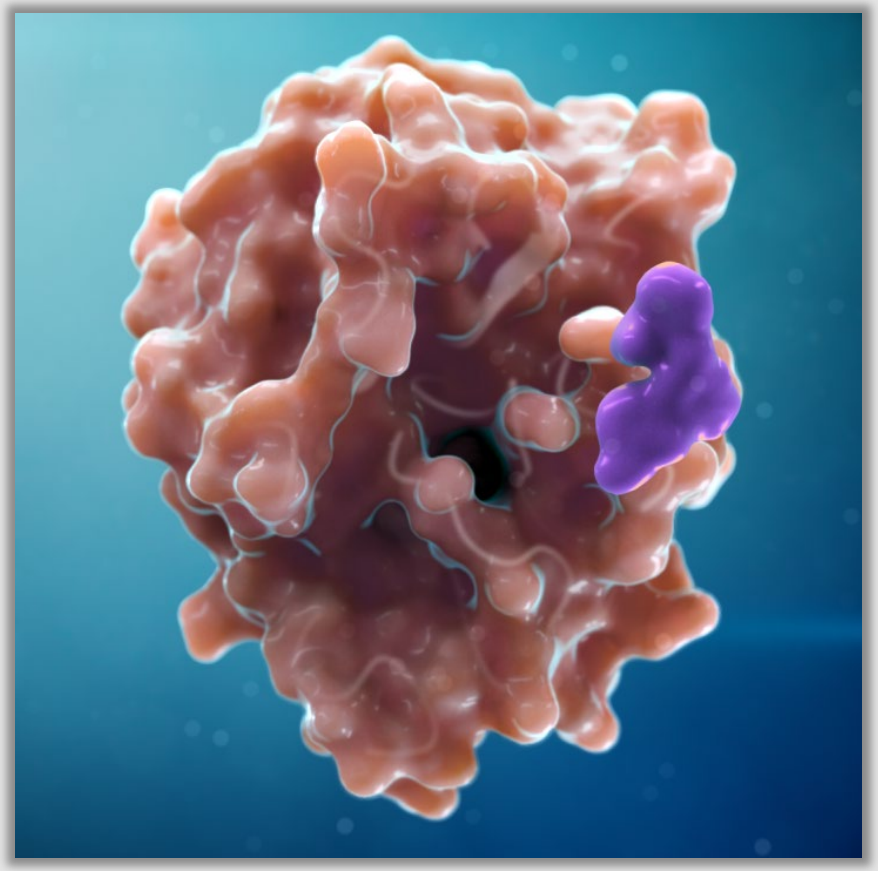
Predictive models
provide a basic understanding of the 3-D protein structure

Visibility to the atomic level

is what BioCryst sees to inform designing a best-in-class drug



UNDERSTANDING HOW A PROTEIN CHANGES SHAPE WHILE MOLECULES BIND TO IT IS CRITICAL

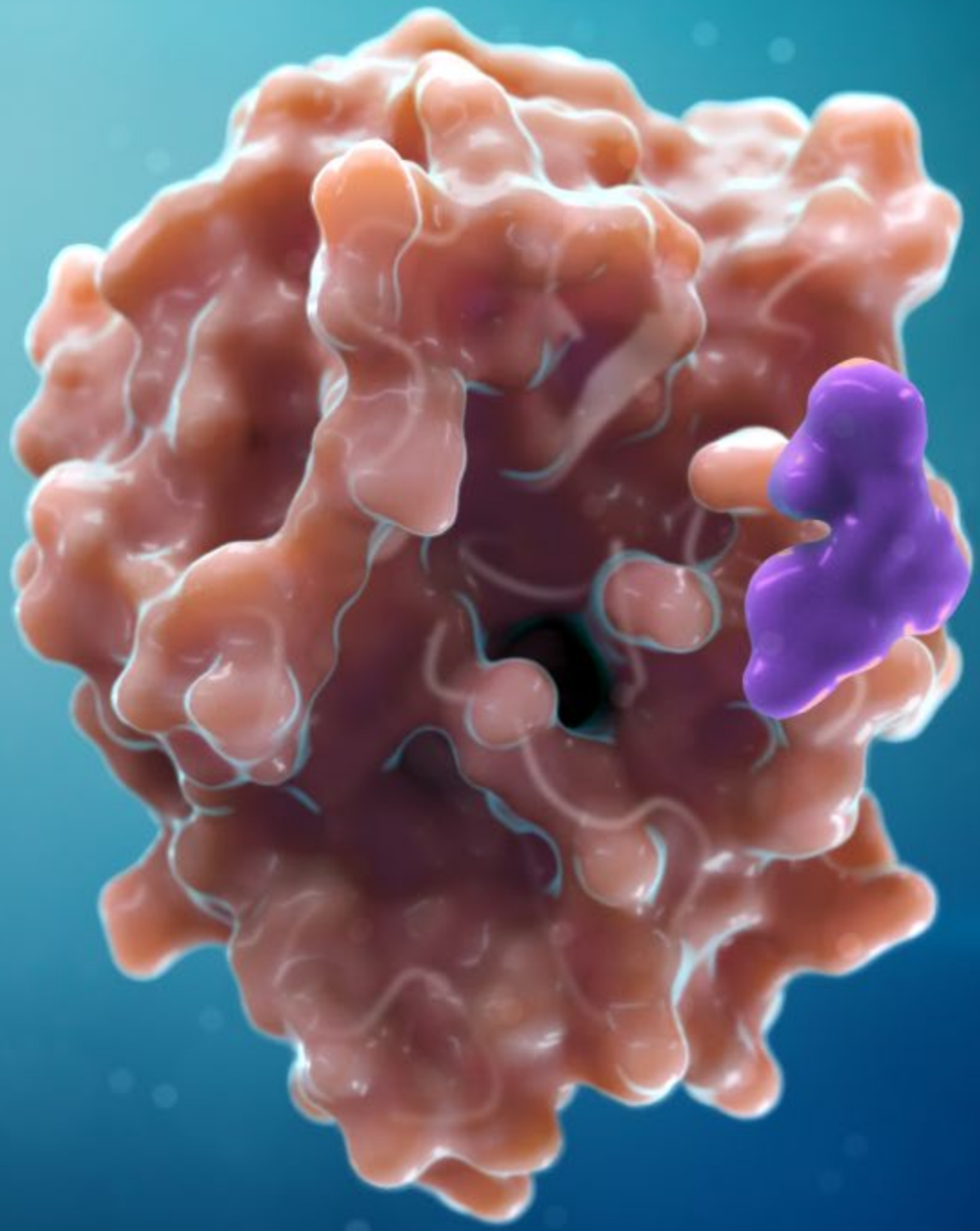


3 Challenges to Overcome

- 3-dimensional protein structure
- High-resolution atomic structure
- Conformational change with binding

Protein active site
is dynamic and continues to change shape after binding

We design our molecules to fit
like a key in a lock



OVERCOMING THE CHALLENGES OF DEVELOPING A FIRST-IN-CLASS OR BEST-IN-CLASS THERAPY

Designing a Molecule

- High potency
- Target specificity
- Bioavailability

3 Challenges to Overcome

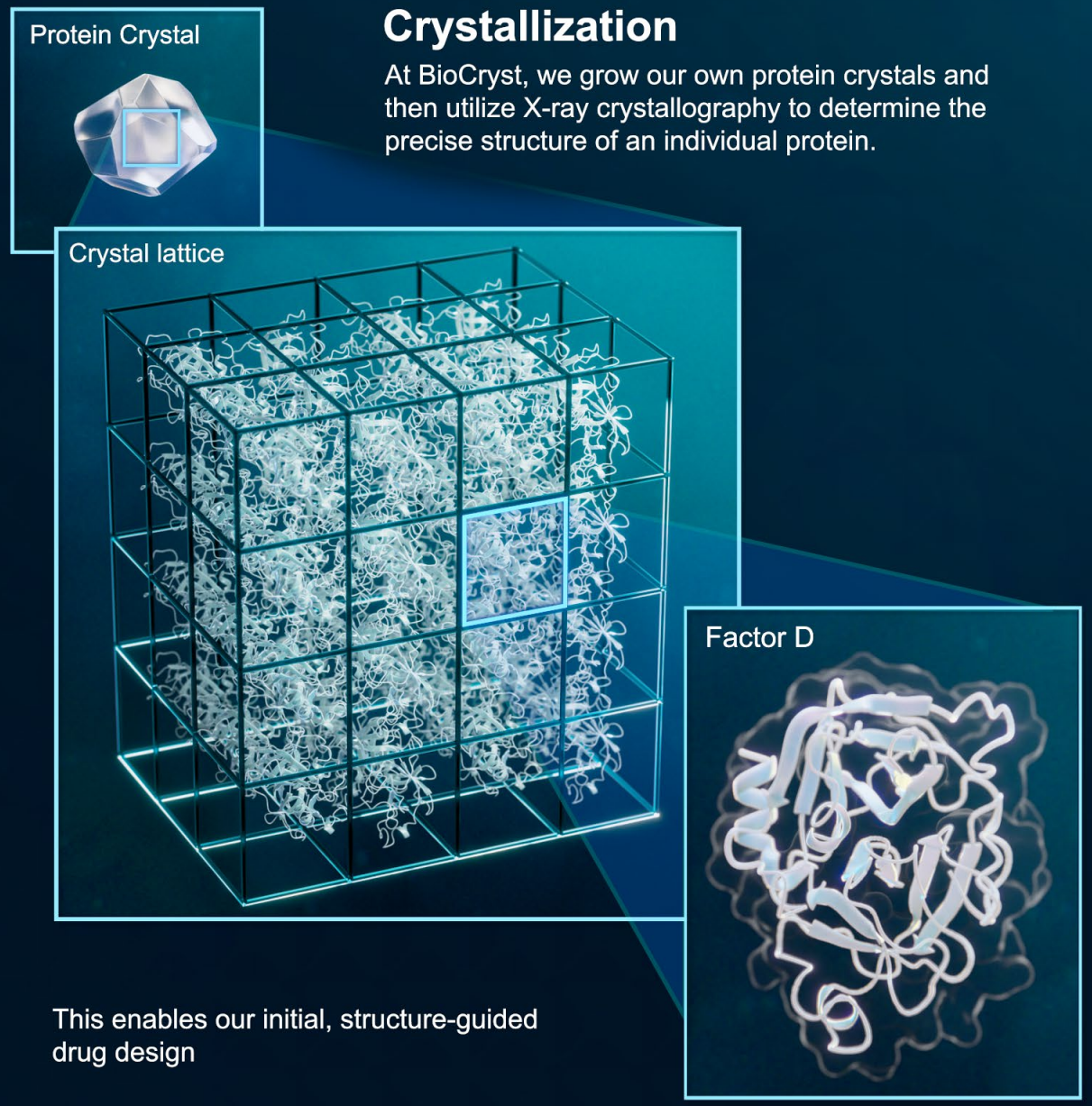
- 3-dimensional protein structure
- High-resolution atomic structure
- Conformational change with binding

Solving for the Challenges

Defining the **high-resolution, 3-D** structure of the protein

Seeing how this structure changes when our drug binds to the active site

Protein Crystallization Approach for Iterative and Potent Drug Design



Crystallization

At BioCryst, we grow our own protein crystals and then utilize X-ray crystallography to determine the precise structure of an individual protein.

This enables our initial, structure-guided drug design

Determining structure at the atomic level

The art and science of protein crystallography

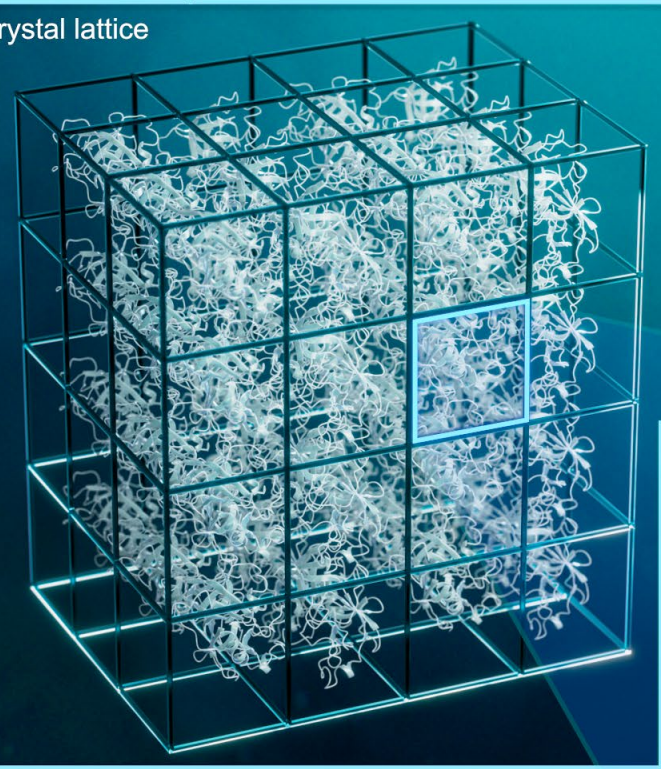
Protein Crystallization Approach for Iterative and Potent Drug Design

Protein Crystal

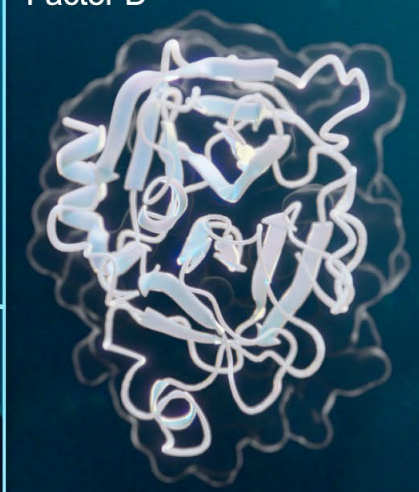
Crystallization

At BioCryst, we grow our own protein crystals and then utilize X-ray crystallography to determine the precise structure of an individual protein.

Crystal lattice



Factor D



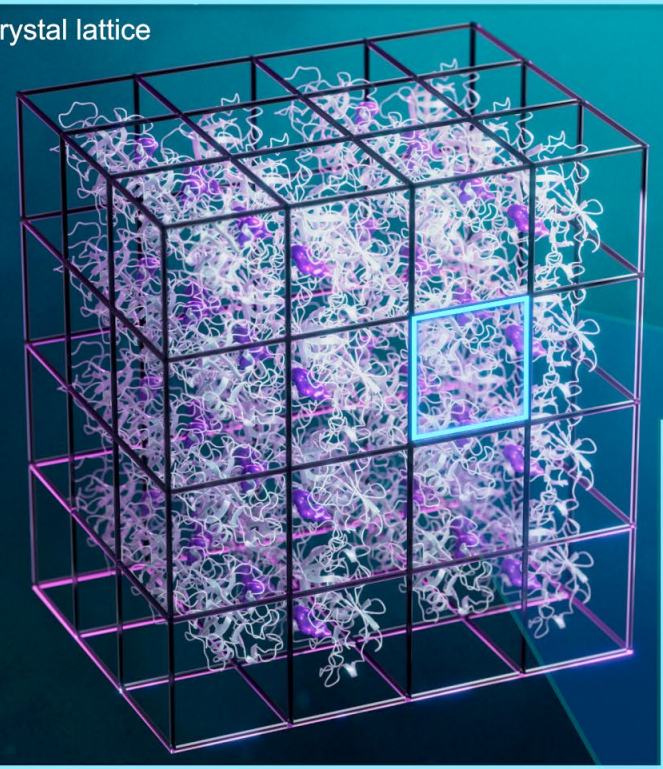
This enables our initial, structure-guided drug design

Protein Crystal

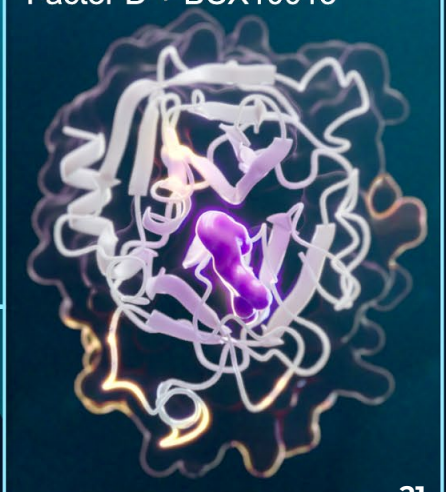
Co-crystallization

When the drug binds to the protein, the protein changes shape. To see these changes, we co-crystallize the protein with the drug bound.

Crystal lattice



Factor D + BCX10013



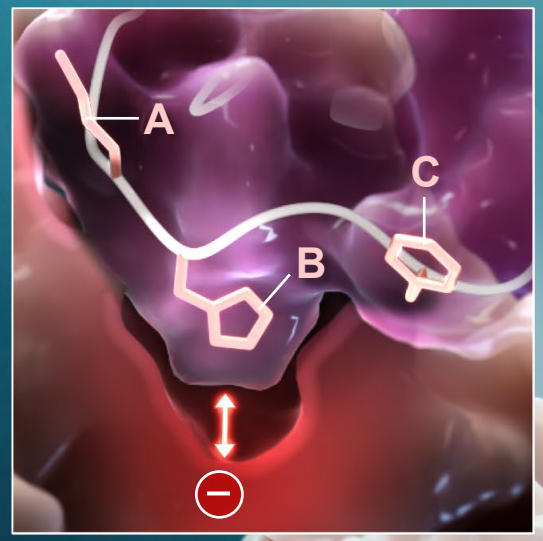
This enables us to iterate on the drug design, accounting for the protein's conformational changes

Expanding our structure-guided approach to generate opportunities in protein therapeutics

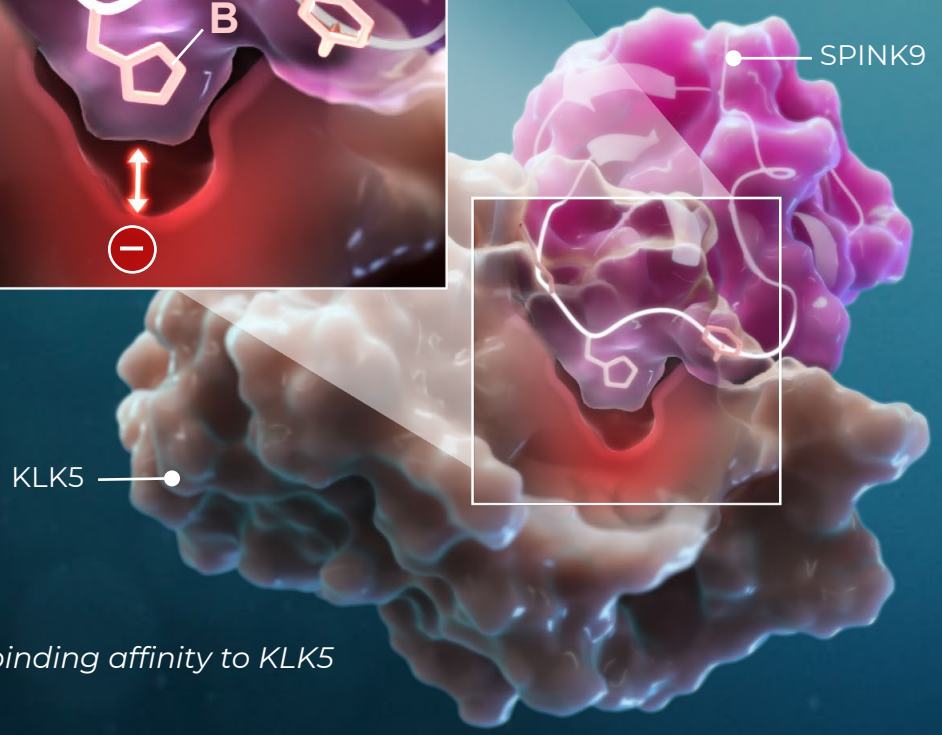
Designing a KLK5 inhibitor for Netherton syndrome

KLK5 Native Ligand: SPINK9

Amino acids (A, B, and C)



- Suboptimal geometric fit
- Empty space in active site
- Limited charge complementarity



Poor binding affinity to KLK5

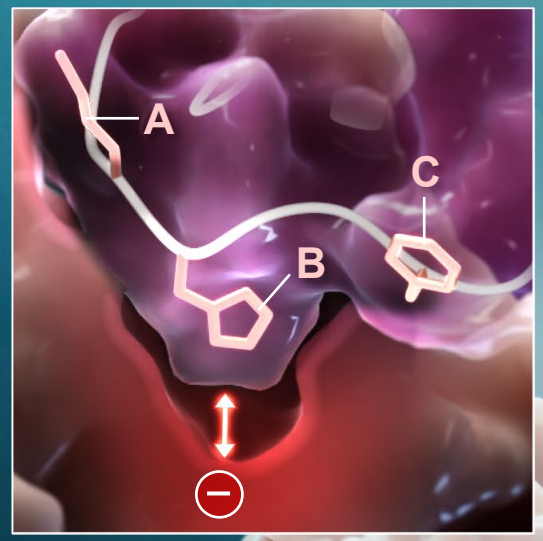
We saw the opportunity to design a better ligand

KLK5, kallikrein 5; SPINK9; serine peptidase inhibitor kazal type 9.

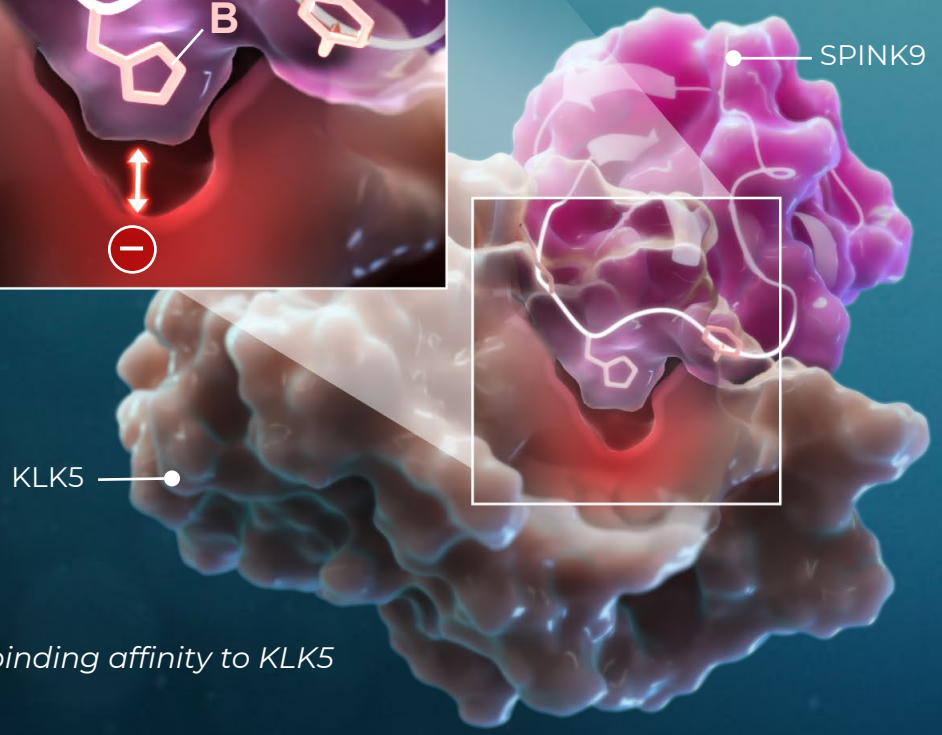
Designing a KLK5 inhibitor for Netherton syndrome

KLK5 Native Ligand: SPINK9

Amino acids (A, B, and C)



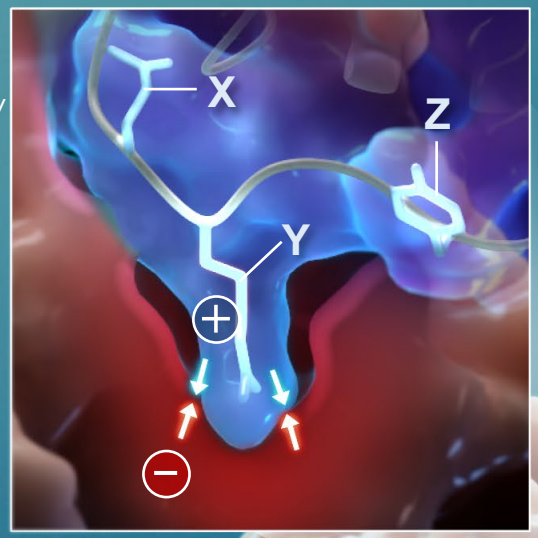
- Suboptimal geometric fit
- Empty space in active site
- Limited charge complementarity



Poor binding affinity to KLK5

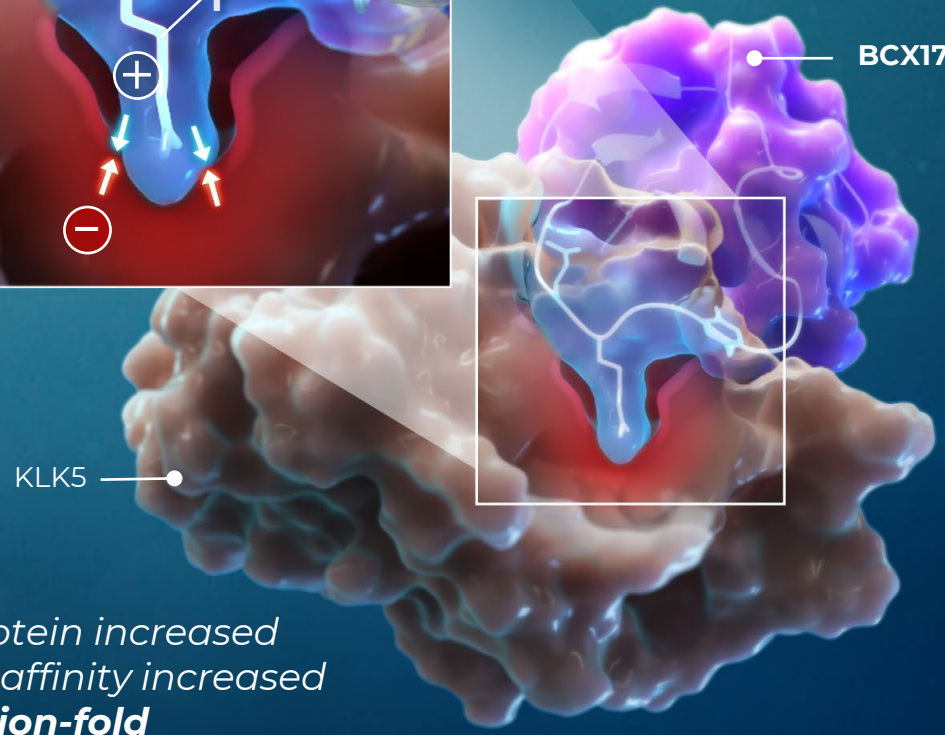
Engineered Protein: BCX17725

Amino acids (X, Y, and Z)



Replaced amino acids for:

- Better geometric fit
- Spatially filled out the active site
- Improved charge complementarity



*Final protein increased binding affinity increased by **1 million-fold***

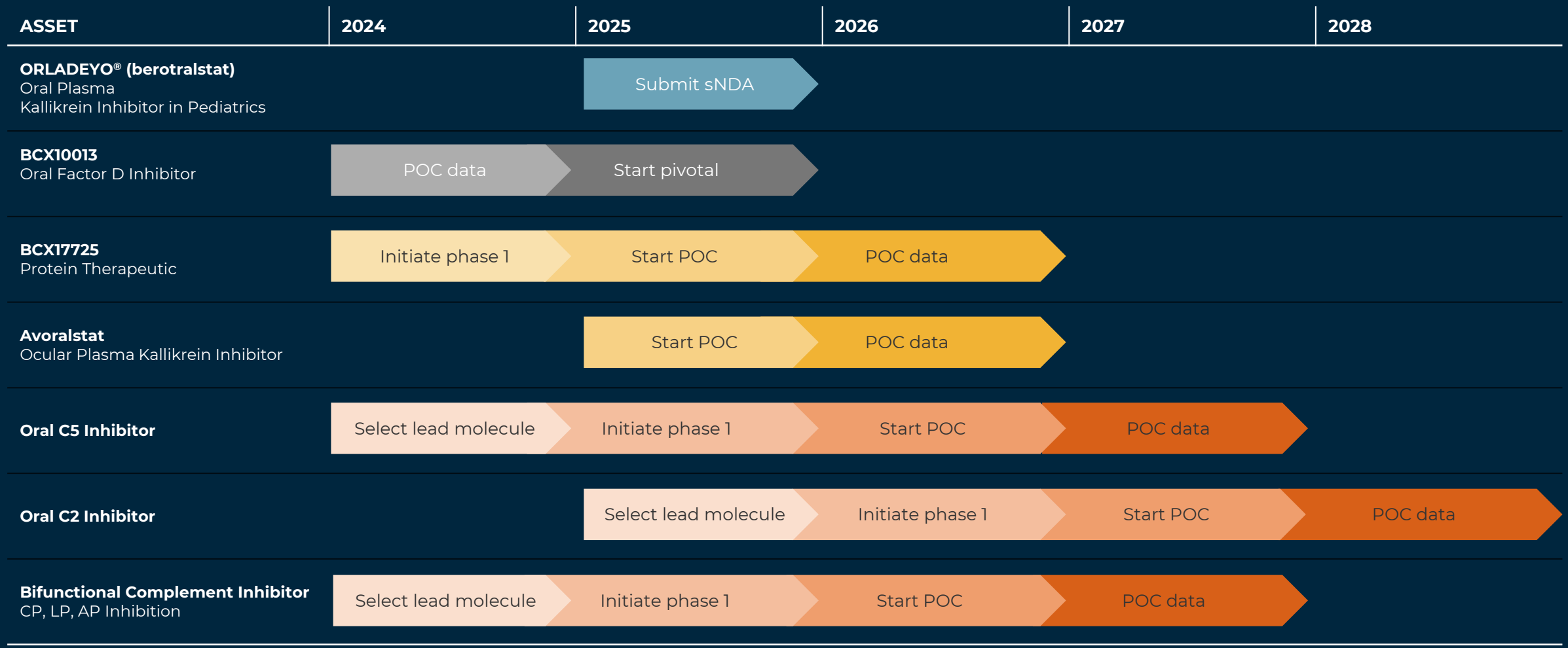
KLK5, kallikrein 5; SPINK9; serine peptidase inhibitor kazal type 9.

OUR BROAD AND DIVERSIFIED 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 in Pediatrics	**Hereditary Angioedema (HAE)**					
BCX10013 Oral Factor D Inhibitor	**Complement-Mediated Diseases**					
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 CP, LP, AP Inhibition	**Complement-Mediated Diseases**					

*Typically Phase 1-2 studies.
†Typically Phase 3 studies.
C5, complement component 5; C2, complement component 2; CP, classical pathway; LP, lectin pathway, AP, alternative pathway.

PIPELINE PROGRAM MILESTONES



AP, alternative pathway; C2, complement component 2; C5, complement component 5;
CP, classical pathway; LP, lectin pathway; POC, proof of concept; sNDA, supplemental new drug application.

ORLADEYO® (BEROTRALSTAT)

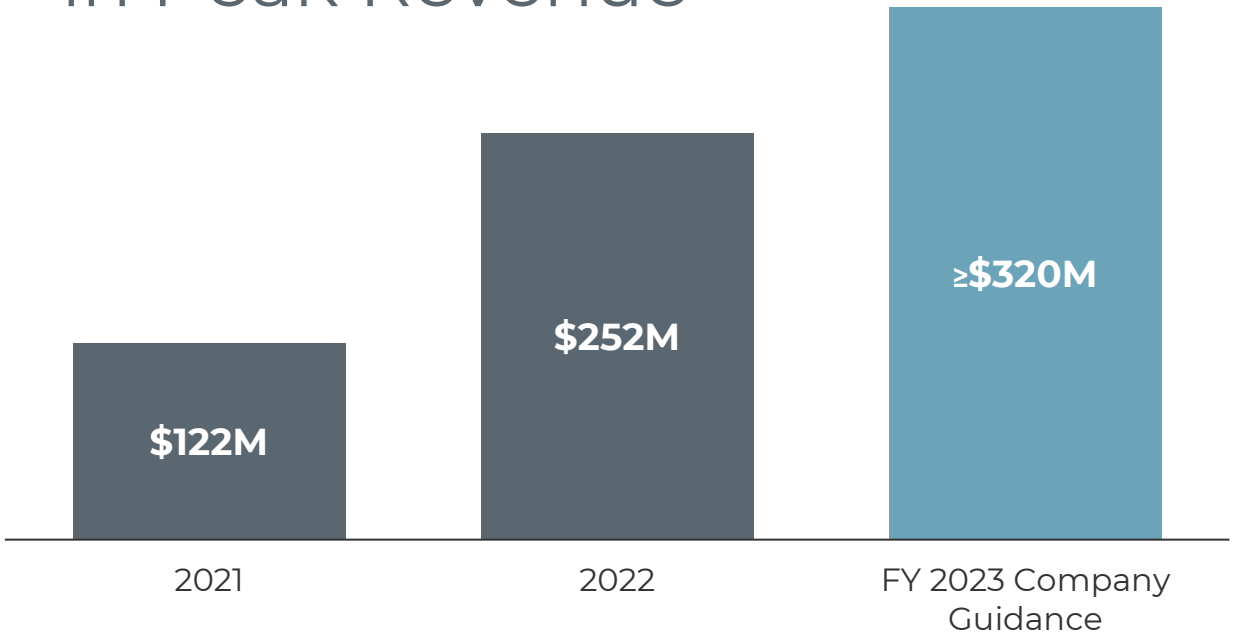
Charlie Gayer, Chief Commercial Officer

ORLADEYO®: THE FIRST AND ONLY ONCE-DAILY ORAL PROPHYLACTIC THERAPY FOR HAE IS ON A PATH TO $1 BILLION PEAK REVENUE

In hereditary angioedema (HAE),
this is big.

In your day,
this is small.

ORLADEYO®:
$1 Billion
in Peak Revenue



FY, fiscal year. 1. BioCryst Pharmaceuticals data on file 2023.

ORLADEYO® FILLS AN UNMET NEED FOR PATIENTS WITH HAE

50% of US patients receiving ORLADEYO® switched from another prophylactic therapy

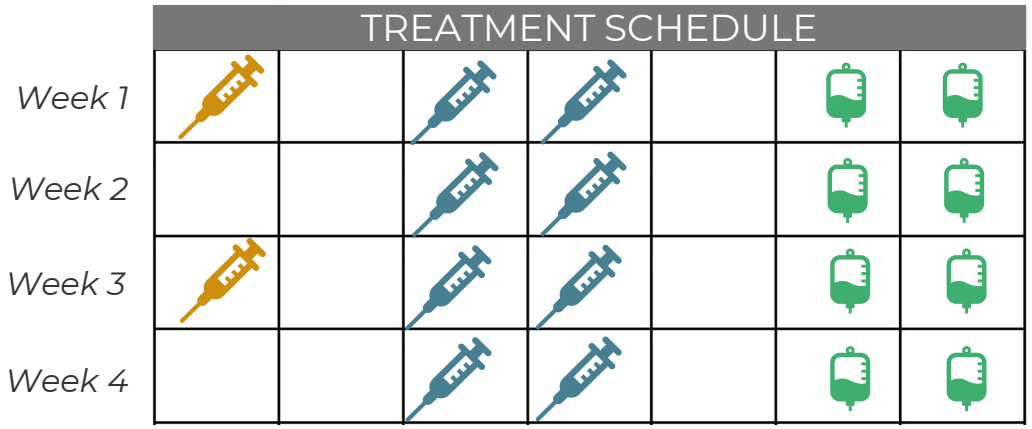
Injectables add treatment burden

- Scheduling
- Preparation and administration
- Complications with travel
- Discomfort

TAKHZYRO[1]: SC injection

HAEGARDA[2]: SC injection

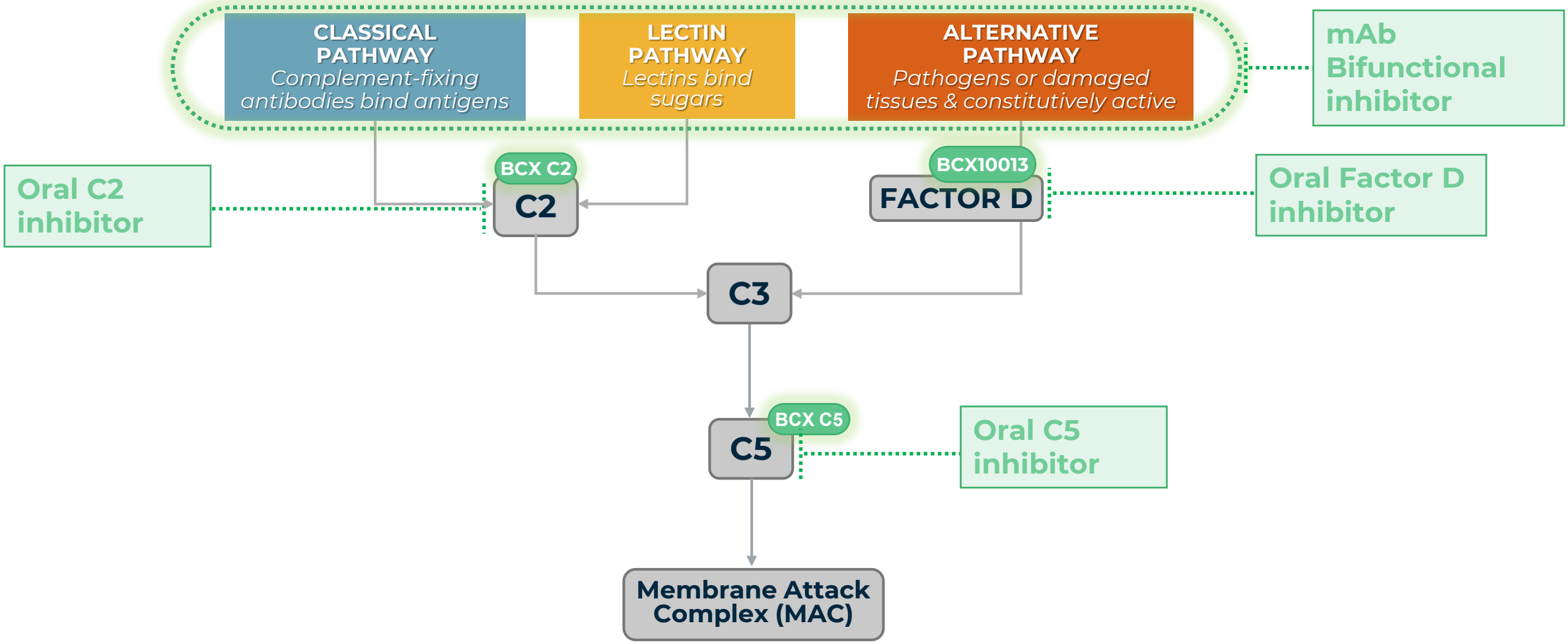
CINRYZE[3]: IV infusion



HAE, hereditary angioedema; IV, intravenous; SC, subcutaneous. 1. Takhzyro [package insert]. Takeda Pharmaceuticals. 2023. 2. Haegarda [package insert]. CSL Behring. 2020. 3. Cinryze [package insert]. ViroPharma Biologics LLC, Takeda Pharmaceuticals. 2022.

COMMERCIAL OPPORTUNITY IN COMPLEMENT-MEDIATED DISEASES

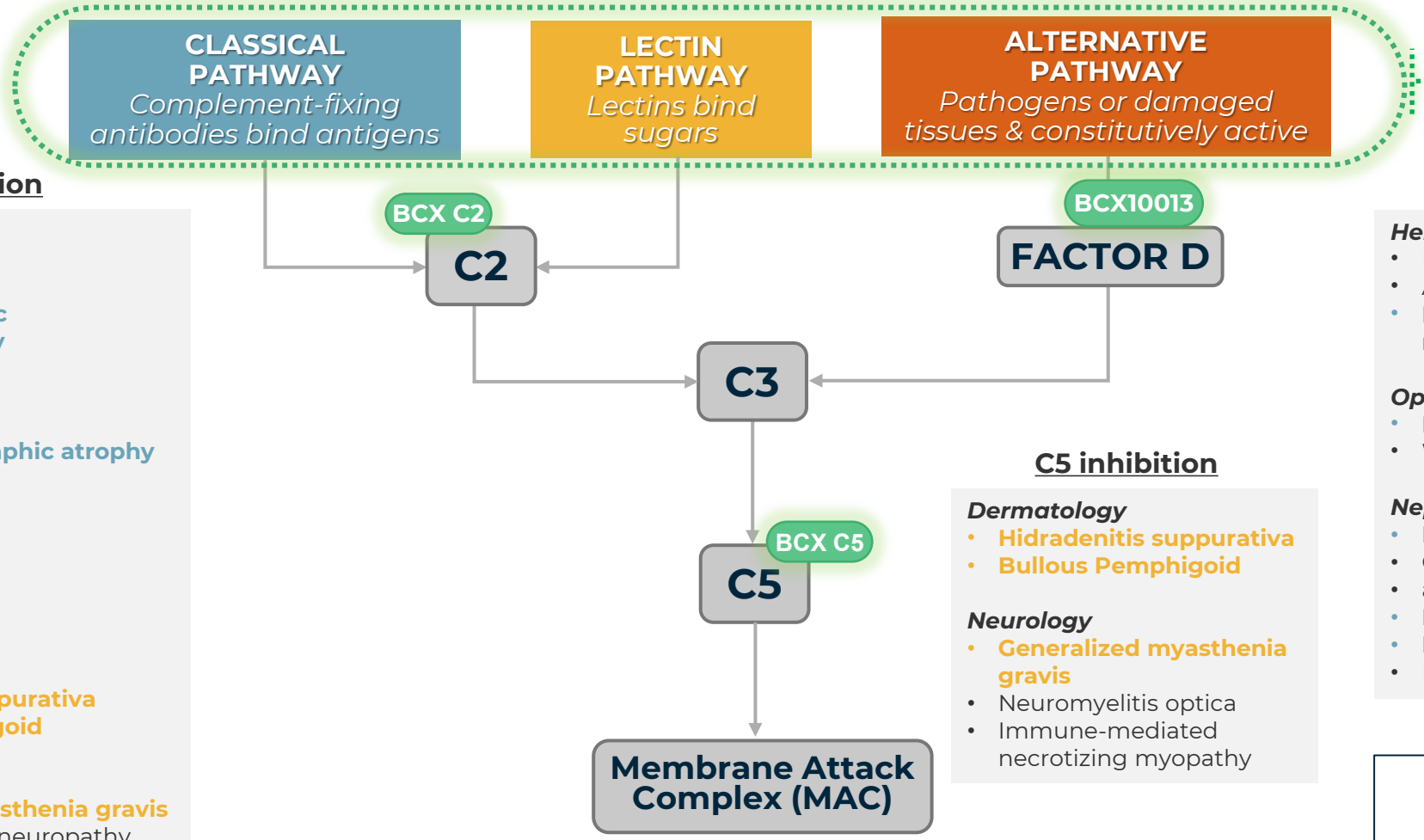
BIOCRYST'S PORTFOLIO OF COMPLEMENT INHIBITORS



C2, complement component 2; C3, complement component 3; C5, complement component 5; mAb, monoclonal antibody.

1. Barratt J. *Front Immunol*. 2021;12:712572. 2. West EE, et al. *Nat Rev Nephrol*. 2023;19(7):426-439.

MANY POTENTIAL OPPORTUNITIES TO HELP PATIENTS WITH UNMET NEEDS



C2 inhibition

Hematology
- CAD
- wAIHA
- HSCT-thrombotic microangiopathy
- ITP

Ophthalmology
- Dry AMD/Geographic atrophy

Nephrology
- IgAN
- IgAV-N
- Lupus nephritis
- PMN

Dermatology
- Hidradenitis suppurativa
- Bullous Pemphigoid

Neurology
- Generalized myasthenia gravis
- Multifocal motor neuropathy
- Guillain-Barré syndrome

C5 inhibition

Dermatology
- Hidradenitis suppurativa
- Bullous Pemphigoid

Neurology
- Generalized myasthenia gravis
- Neuromyelitis optica
- Immune-mediated necrotizing myopathy

Factor D inhibition

Hematology
- PNH
- ANCA-V
- HSCT-thrombotic microangiopathy

Ophthalmology
- Dry AMD/Geographic atrophy
- Wet AMD

Nephrology
- IgAN
- C3G
- aHUS
- IgAV-N
- Lupus nephritis
- PMN

Combination therapy legend:

C2 + Factor D inhibition
C2 + C5 inhibition

aHUS, atypical hemolytic uremic syndrome; AMD, age-related macular degeneration; ANCA-V, antineutrophilic cytoplasmic antibody vasculitis; C2, complement component 2; C3, complement component 3; C5, complement component 5; C3G, C3 glomerulopathy; CAD, cold agglutinin disease; DME, diabetic macular edema; HSCT, hematopoietic stem cell transplant; IgAN, IgA nephropathy; IgAV-N, IgA vasculitis-nephritis; ITP, immune thrombocytopenia purpura; mAb, monoclonal antibody; PMN, primary membranous nephropathy; PNH, paroxysmal nocturnal hemoglobinuria; wAIHA, warm autoimmune hemolytic anemia.1. Barratt J. *Front Immunol*. 2021;12:712572. 2. West EE, et al. *Nat Rev Nephrol*. 2023;19(7):426-439.

ORAL C5 INHIBITOR AS POTENTIAL THERAPY FOR GENERALIZED MYASTHENIA GRAVIS

Target Profile

- First targeted oral for generalized myasthenia gravis (gMG) with competitive efficacy to injected and infused therapies

Opportunities

- Switch from infused therapies
- Earlier use in treatment paradigm

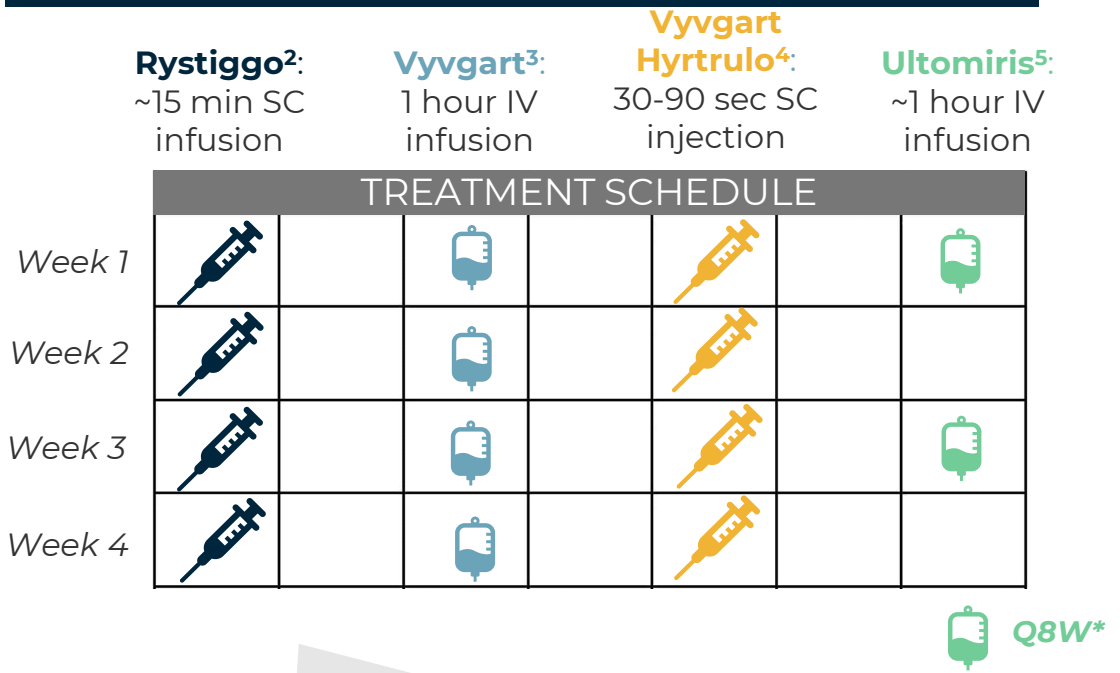
US Patient Population[1]

- Overall: ~70K, 80-85% AChR+
- Refractory steroids and ISTs: 5K-10K

Sales Estimates[6]

- $2.3B in 2023
- $6.1B in 2028

Competition



*"A key unmet need is to have a **high efficacy drug** like Ultomiris or Vyvgart but **in oral form**. It would make it much easier with taking it long-term than to keep going to an infusion center or having a nurse come for hours to your house to do it."*

– US Neurologist[7]

*Maintenance dosing begins 2 weeks after the initial loading dose and occurs once every 4 or 8 weeks depending on body weight; AChR+, positive acetylcholine receptor antibody; C5, complement component 5; ISTs, immunosuppressive therapies; IV, intravenous; Q8W, once every 8 weeks; SC, subcutaneous; US, United States.

1. Dresser et al. J Clin Med. 2021; Myasthenia Gravis Foundation of America; 2. Rystiggo [package insert]. UCB, Inc. 2023. 3. Vyvgart [package insert]. argenx. 2021. 4. Vyvgart Hytrulo [package insert]. argenx. 2023. 5. Ultomiris [package insert]. Alexion Pharmaceuticals. 2022. 6. Evaluate Pharma. 7. BioCryst Pharmaceuticals Market Research Q2 2023.

ORAL C2 INHIBITOR AS POTENTIAL THERAPY FOR AUTOIMMUNE HEMOLYTIC ANEMIAS

Target Profile

- First-in-class oral C2 inhibitor

Opportunities

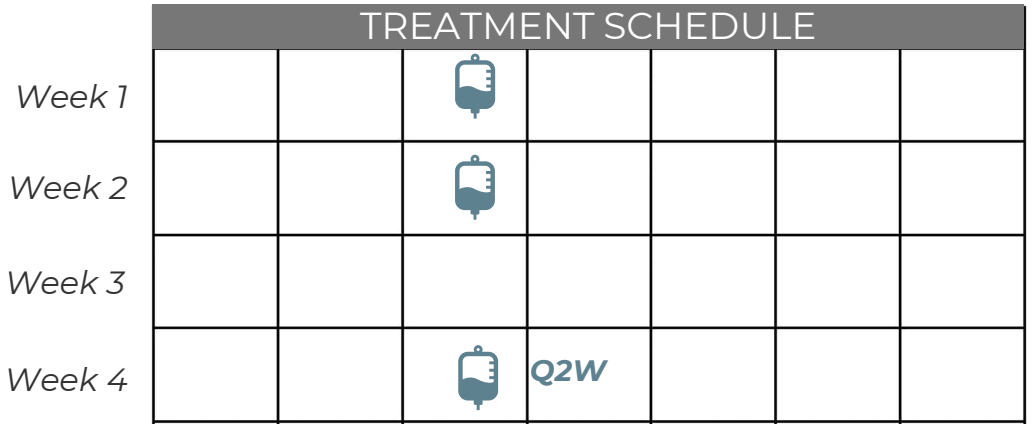
- Switch from infused therapies
- Earlier use in treatment paradigm
- Potential first targeted therapy (wAIHA)

US Patient Population

- Cold agglutinin disease (CAD)[1,2]: 5K
- Warm autoimmune hemolytic anemia (wAIHA)[3,4]: 25K

Competition

Enjaymo[5] (C1s inhibitor):
1 hour IV infusion for CAD



ARGX-117, an intravenous C2 inhibitor, is in phase 2 for multifocal motor neuropathy (MMN)[6]

C2, complement component 2; IV, intravenous; Q2W, once every 2 weeks. 1. Berensten et al. Hematologica. 2006;91(4):460-6. 2. Mullins et al. Blood Adv. 2017;1(13):839-848. 3. Kalfa et al. Hematology Am Soc Hematol Educ Program. 2016;2016(1):690-697. 4. Tranekaer et al. J Clin Med. 2021;10(6);1244. 5. Enjaymo [package insert]. Bioverativ USA Inc, Sanofi. 2023; 6. https://www.us.argenx.com/pipeline#immunology-solutions.

BCX10013 AS POTENTIAL THERAPY FOR KIDNEY DISEASES

Target Profile

- Best-in-class AP inhibitor with once-daily dosing and efficacy similar to iptacopan

Opportunities

- Potential standard of care complement inhibitor (both)
- Earlier use in treatment paradigm (IgAN)

US Patient Population

- Immunoglobulin A nephropathy (IgAN)[1]: ~160K overall, ~30K high risk of progression[2]
- C3 glomerulopathy (C3G)[3]: ~6K

Competition

- Iptacopan, a twice-daily oral factor B inhibitor, is in phase 3 for IgAN and C3G
- Pegcetacoplan, a twice-weekly subcutaneous infusion, is in phase 3 for C3G

"I like the new MOA, it's unique [and] something I can use to complement my current treatment of IgAN."
– US Nephrologist[2]

"[BCX10013] is a targeted therapy for C3G, that's what we need. We've been dabbling with all kinds of immunosuppression. This takes you to why C3G is happening."
– US Nephrologist[2]

AP, alternative pathway; 1. Schena et al. Epidemiology of IgA Nephropathy: A Global Perspective. Sem Nehprol. 2018.. 2. BioCryst Pharmaceuticals Market Research Q2 2022. 3. Medjeral-Thomas NR et al. C3 Glomerulopathy: Clinicopathologic Features and Predictors of Outcome. Clin J Am Soc Nephrol. 2014;9(1):46-53.

BIFUNCTIONAL COMPLEMENT INHIBITOR AS POTENTIAL THERAPY FOR KIDNEY DISEASES

Target Profile

- First-in-class combo inhibitor of CP, LP, AP, as a low-volume, subcutaneous injection

Opportunities

- Best-in-class 2L or 3L treatment for patients at high risk or refractory to SoC due to multiple complement pathway involvement

US Patient Population

- Immunoglobulin A nephropathy (IgAN)[1]: ~160K overall, ~30K high risk of progression[2]
- Lupus nephritis (LN)*[3,4,5]: 55K, up to 30K addressable[6-11]

Competition

- KP104 (C5+factor H inhibitor) from Kira Pharmaceuticals is in phase 2 for systemic lupus erythematosus, IgAN and PNH[12]
- GL-0719 (CP + LP inhibitor) from Gliknik is in a phase 1 trial[13]

*Prevalance reflects patients with Class III/IV disease. 2L, second-line; 3L, third-line; C5, complement component 5; AP, alternative pathway; CP, classical pathway; LP, lectin pathway; SoC, standard of care.1. Schena et al. Epidemiology of IgA Nephropathy: A Global Perspective. Sem Nehprol. 2018. 2. BioCryst Pharmaceuticals Market Research Q2 2022. 3. GlobalData; Cantor Research on LN from September 2021. 4. JonesTrading Equillium (Mar 2021). 5. Wedbush Nephrology Survey. 6. Cantor Fitzgerald Research on LN (Sep 2021). 7. Jones Trading Equillium (March 2021). 8. Wedbush Nehrology Survey (Feb 2023). 9. Tektonidou et al. Arthritis & Rheumatology. 2016. 10. Yo et al. Open Access Rheumatology. 2019. 11. Kalloo et al. 2013. 12. https://www.kirapharma.com/pipeline. 13. https://www.gliknik.com/gl-0719/.

MULTIPLE PATHS TO COMPLEMENT MARKET LEADERSHIP

01 Best-in-class for ultra-rare disease

02 First-in-class oral in injectable/infused market

03 First-/best-in-class for patients needing combo therapy within larger disease populations

04 Potential to help more patients at different stages of disease pathology or progression

05 Diverse portfolio spreads development risk and increases commercial opportunity

Multiple programs, small molecule and protein therapeutics, applicable to many diseases

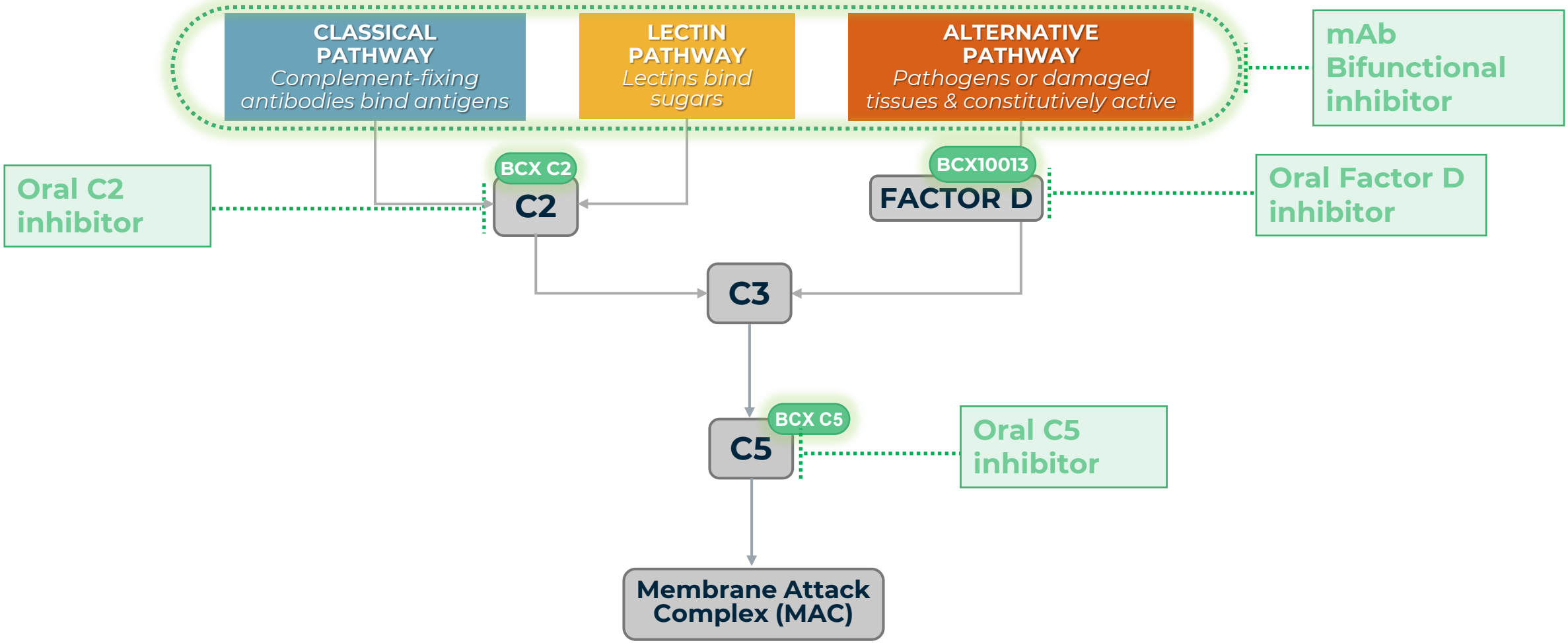
Disease	BCX10013	C5	C2	Bi-functional
IgAN	✓		✓	✓
gMG		✓	✓	✓
CAD	✓		✓	✓
LN	✓		✓	✓
C3G	✓			
wAIHA			✓	

C2, complement component 2; C3G, C3 glomerulopathy; C5, complement component 5; CAD, cold agglutinin disease; IgAN, Immunoglobulin A nephropathy; LN, lupus nephritis; gMG, generalized myasthenia gravis; wAIHA, warm autoimmune hemolytic anemia.

SPOTLIGHT ON COMPLEMENT DISEASES

Dr. Bill Sheridan, Chief Development Officer

BIOCRYST'S PORTFOLIO OF COMPLEMENT INHIBITORS



C2, complement component 2; C3, complement component 3; C5, complement component 5; mAb, monoclonal antibody.

1. Barratt J. *Front Immunol*. 2021;12:712572. 2. West EE, et al. *Nat Rev Nephrol*. 2023;19(7):426-439.

OVERVIEW OF BIOCRYST COMPLEMENT PROGRAM

- Developing 4 programs to create a comprehensive portfolio of single pathway and multiple pathway complement inhibitors
- Goals for each program are first-in-class or best-in-class
- This approach creates opportunity to treat many complement-mediated diseases across multiple therapeutic areas
- We aim to start 3 NME phase 1 studies, deliver POC results for 3 programs, and start 1 pivotal study in the next 4 years

AP, alternative pathway; C2, complement component 2; C5, complement component 5; CP, classical pathway; IND, investigational new drug; LP, lectin pathway; NME, new molecular entity; POC, proof of concept.

C5 INHIBITOR: FIRST-IN-CLASS ORAL INHIBITOR

OUR BROAD AND DIVERSIFIED 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 in Pediatrics	**Hereditary Angioedema (HAE)**					
BCX10013 Oral Factor D Inhibitor	**Complement-Mediated Diseases**					
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 CP, LP, AP Inhibition	**Complement-Mediated Diseases**					

*Typically Phase 1-2 studies.
†Typically Phase 3 studies.
C5, complement component 5; C2, complement component 2; CP, classical pathway; LP, lectin pathway, AP, alternative pathway.

TARGETING C5 HAS BEEN THOROUGHLY VALIDATED AS A SUCCESSFUL THERAPEUTIC STRATEGY IN SEVERAL INDICATIONS

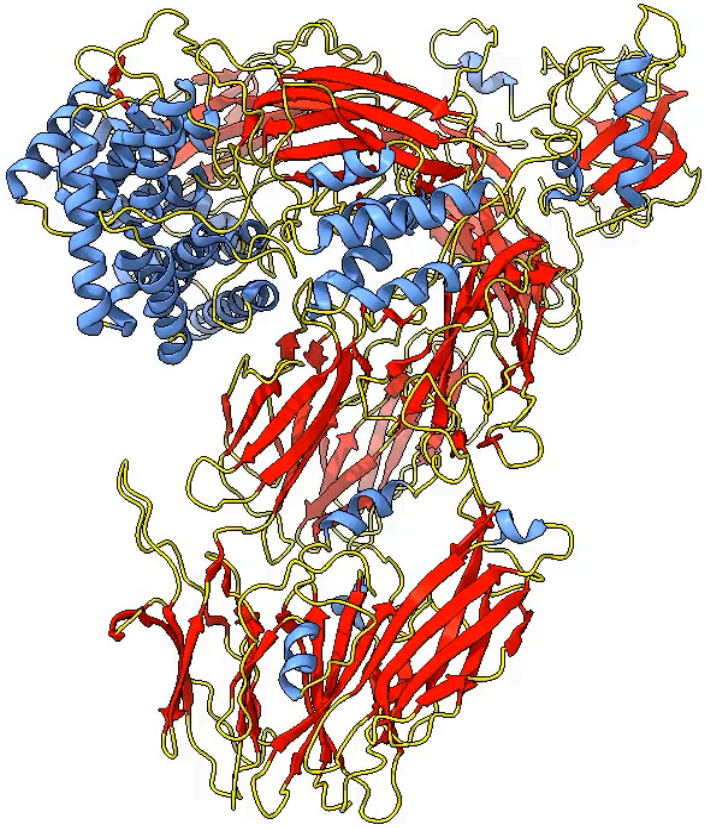
C5 is the initiator
of the terminal phase for **all 3 complement pathways.**[1]

For all complement pathways, C5 activation leads to the formation of the **membrane attack complex (MAC).**[1]

C5 activation also leads to production of **C5a, an anaphylatoxin** that triggers inflammation.[1,2]

Inhibiting C5 is a promising therapeutic approach for multiple complement-mediated disorders including **gMG, PNH, aHUS, NMOSD, and ANCA-V, among others.**[1,2]

Structure of Human Complement C5

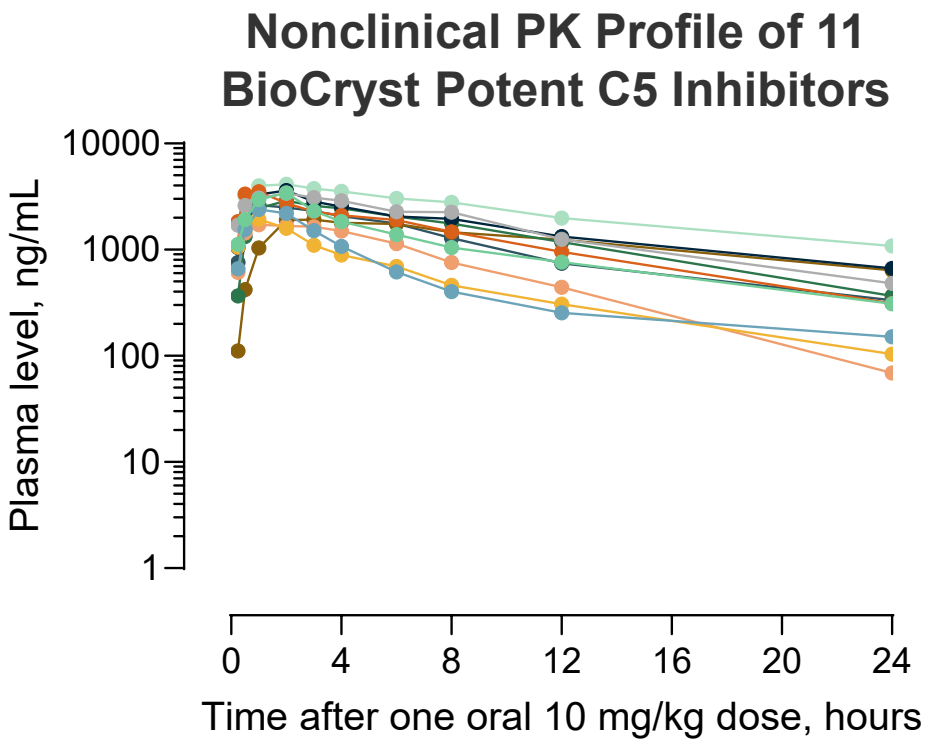


aHUS, atypical hemolytic uremic syndrome; ANCA-V, antineutrophilic cytoplasmic antibody associated vasculitis; C5, complement component 5; C5a, complement component 5a; gMG, generalized myasthenia gravis; NMOSD, neuromyelitis optica spectrum disorder; PNH, paroxysmal nocturnal hemoglobinuria. 1. Giorgio C, et al. *Biomedicines.* 2021;9(399):1-18. 2. Mantegazza R, et al. *ImmunoTargets and Therapy.* 2020;9:317-331.

LEAD OPTIMIZATION OF AN ORAL SMALL MOLECULE C5 INHIBITOR IS PROGRESSING RAPIDLY TO IND CANDIDATE SELECTION

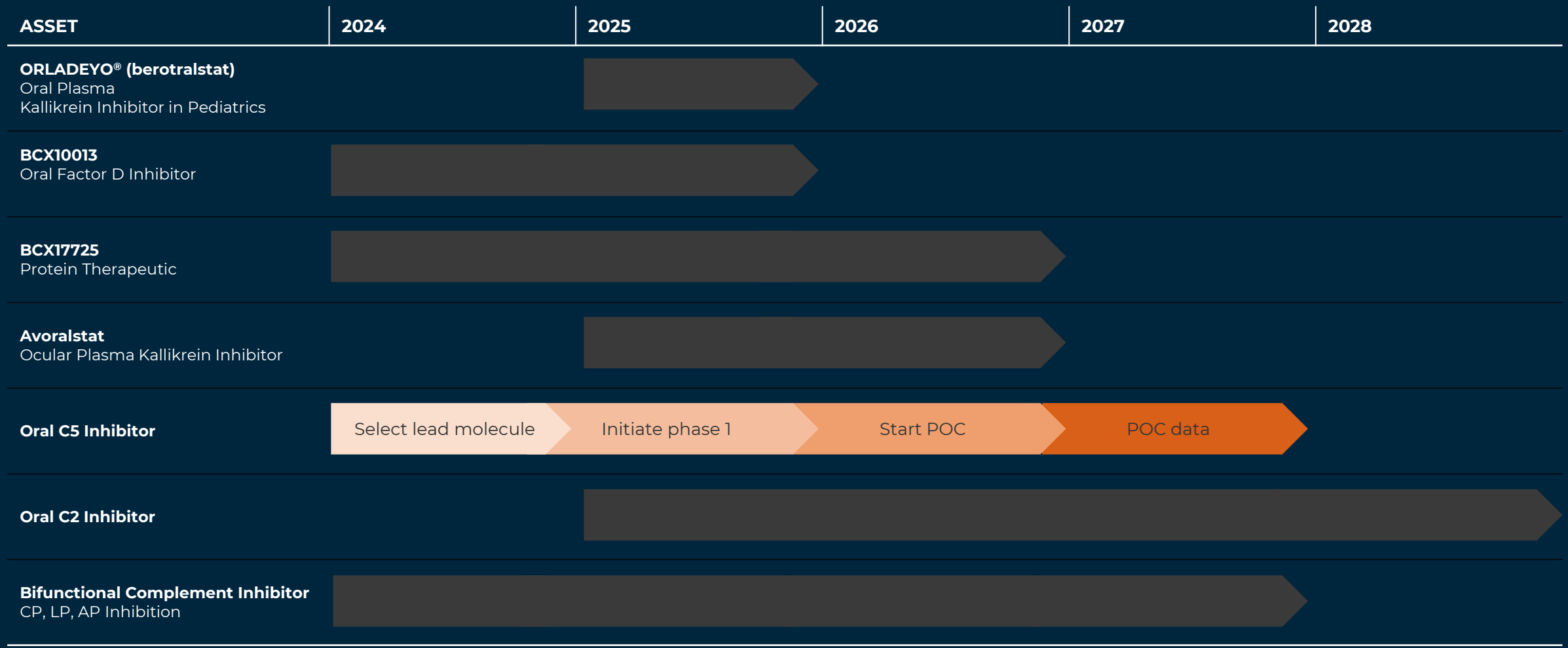
Goals are **high potency**, **selectivity**, **oral bioavailability**, **sustained exposure**, favorable metabolic profile, and typical small molecule physicochemical properties.

Potency	Inhibition assay for cell lysis by MAC which is dependent on the cleavage/breakup of **C5 IC_{50} < 10 nM**
Selectivity	Low risk of off-target effects
Oral bioavailability	**F > 40%,** similar to marketed small molecule therapeutics
Sustained exposure	C_{24}/IC_{50} ratio > 10, **predictive of sustained PD effect**
Physicochemical properties	**MW < 500 D,** typical of other oral small molecules



C_{24}, concentration 24 hours post-dose; C5, complement component 5; D, Dalton; F, oral bioavailability; IC_{50}, half maximum inhibitor concentration; IND, investigational new drug; MAC, membrane attack complex; MW, molecular weight; nM, nanomolar; PD, pharmacodynamic; RBC, red blood cell. BioCryst Pharmaceuticals data on file 2023.

PIPELINE PROGRAM MILESTONES



AP, alternative pathway; C2, complement component 2; C5, complement component 5;
CP, classical pathway; LP, lectin pathway; POC, proof of concept; sNDA, supplemental new drug application.

C2 PROGRAM: A FIRST-IN-CLASS ORAL SERINE PROTEASE INHIBITOR TO BLOCK BOTH THE CLASSICAL AND LECTIN PATHWAYS

OUR BROAD AND DIVERSIFIED 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 in Pediatrics	**Hereditary Angioedema (HAE)**					
BCX10013 Oral Factor D Inhibitor	**Complement-Mediated Diseases**					
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 CP, LP, AP Inhibition	**Complement-Mediated Diseases**					

*Typically Phase 1-2 studies.
†Typically Phase 3 studies.
C5, complement component 5; C2, complement component 2; CP, classical pathway; LP, lectin pathway, AP, alternative pathway.

COMPLEMENT-FIXING IgG AND IgM (CP) OR LECTIN-ACTIVATING IgG_4 AUTOANTIBODY (LP) DISEASES ARE KEY TARGETS FOR C2 BLOCKADE

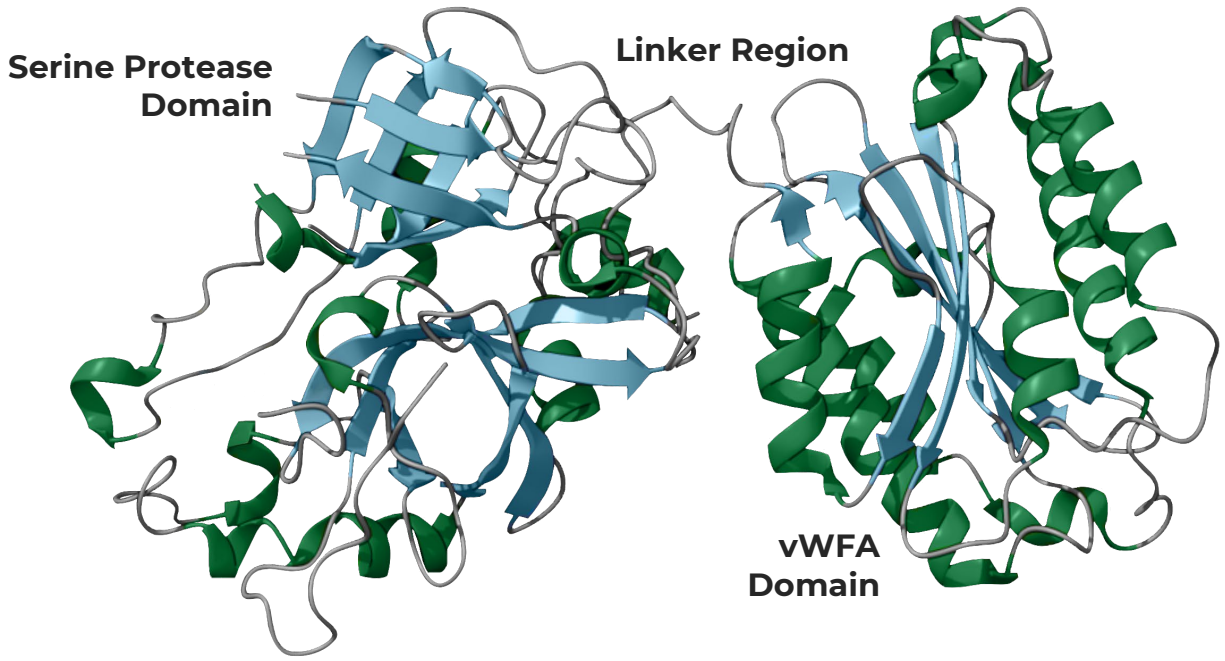
C2 is a serine protease that provides catalytic activity for the C3 and C5 convertases of the **classical and lectin complement pathways.**[1]

Inhibiting C2 can decrease inflammation in complement-mediated diseases by blocking the classical and lectin pathways.[2]

Developing an oral **small molecule inhibitor of C2,** while challenging, would be highly valuable.

Blocking the CP and/or LP is a promising approach for several diseases, including **bullous pemphigoid and autoimmune hemolytic anemias.**[2,3]

Structure of Human Complement C2a



C2, complement component 2; C2a, complement component 2a; C5, complement component 5; CP, classical pathway; IgG, immunoglobulin G; IgG_4, immunoglobulin G4; IgM, immunoglobulin M; LP, lectin pathway. 1. Krishnan V, et al. *Act Cryst.* 2009;D65:266-274. 2. Berentsen S. *Transfus Med Hemother*. 2015;42:303-310. 3. Papara C, et al. *Front. Immunol*. 2022;13:973702.

THE ORAL SMALL MOLECULE C2 INHIBITOR PROJECT IS PROGRESSING THROUGH LEAD IDENTIFICATION

Goals are **high potency**, **selectivity**, **oral bioavailability**, **sustained exposure**, favorable metabolic profile, and typical small molecule physicochemical properties.

Potency	CP inhibition assay **IC_{50} < 10 nM**
Selectivity	Low potency against other serine proteases, **>1,000-fold less potent than for C2**
Oral bioavailability	F **> 40%**
Sustained exposure	C_{24}/IC_{50} ratio **> 10**
Physicochemical properties	MW **< 500 D**

C2, complement component 2; C_{24}, concentration 24 hours post-dose; CP; classical pathway; D, Dalton; F, oral bioavailability; IC_{50}, half maximum inhibitor concentration; MW, molecular weight; nM, nanomolar. BioCryst Pharmaceuticals data on file.

PIPELINE PROGRAM MILESTONES

AP, alternative pathway; C2, complement component 2; C5, complement component 5;
CP, classical pathway; LP, lectin pathway; POC, proof of concept; sNDA, supplemental new drug application.

BCX10013: BEST-IN-CLASS, ONCE-DAILY, ORAL FACTOR D INHIBITOR TO BLOCK THE ALTERNATIVE PATHWAY

OUR BROAD AND DIVERSIFIED 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 in Pediatrics	**Hereditary Angioedema (HAE)**					
BCX10013 Oral Factor D Inhibitor	**Complement-Mediated Diseases**					
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Avoralstat Ocular Plasma Kallikrein Inhibitor	**Diabetic Macular Edema (DME)**					
Oral C5 Inhibitor	**Complement-Mediated Diseases**					
Oral C2 Inhibitor	**Complement-Mediated Diseases**					
Bifunctional Complement Inhibitor CP, LP, AP Inhibition	**Complement-Mediated Diseases**					

*Typically Phase 1-2 studies.
†Typically Phase 3 studies.
C5, complement component 5; C2, complement component 2; CP, classical pathway; LP, lectin pathway, AP, alternative pathway.

BCX10013 IS A POTENTIAL BEST-IN-CLASS, ONCE-DAILY, ORAL FACTOR D INHIBITOR FOR AP-MEDIATED DISEASES

Several diseases are now known to be driven by **dysregulation of the alternative pathway.**[1]

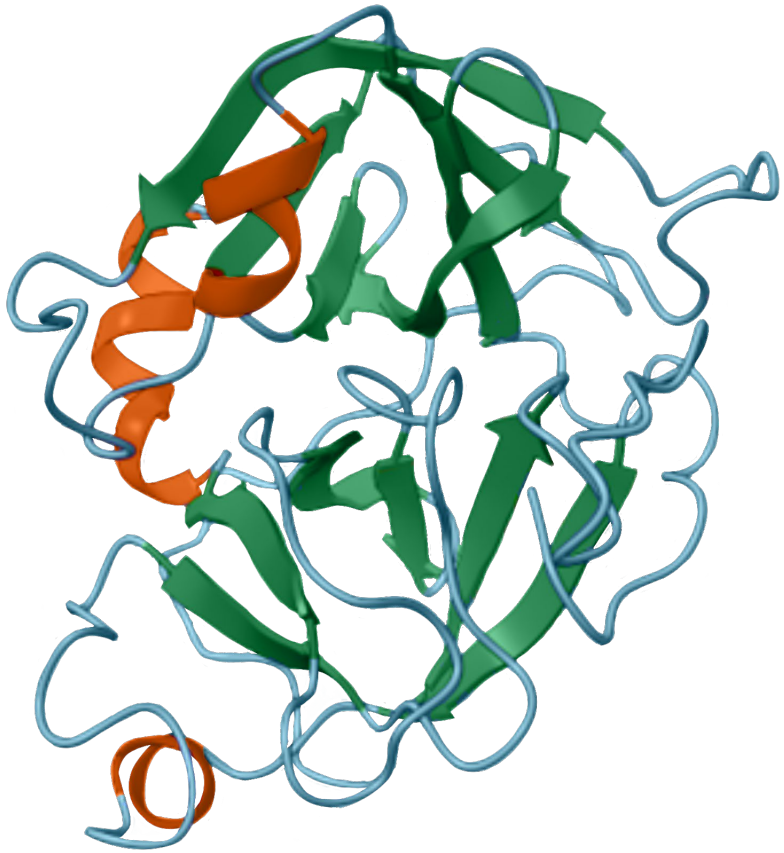
Factor D initiates the first step in the alternative pathway of complement and amplifies complement signaling.[1]

Factor D is a **promising therapeutic target** for several complement-mediated diseases.[1,2]

- IgAN, C3G, PNH, aHUS

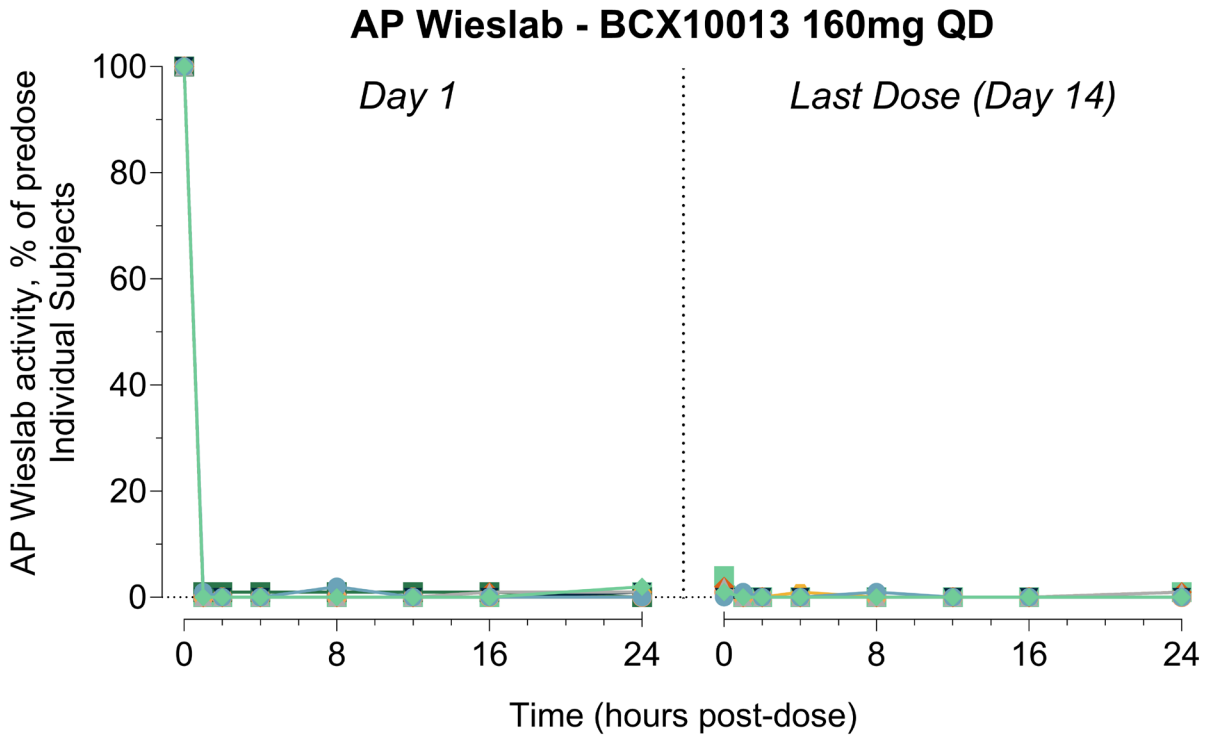
BCX10013, an investigational, **oral Factor D inhibitor**, is being studied in a dose-ranging trial in patients with PNH.

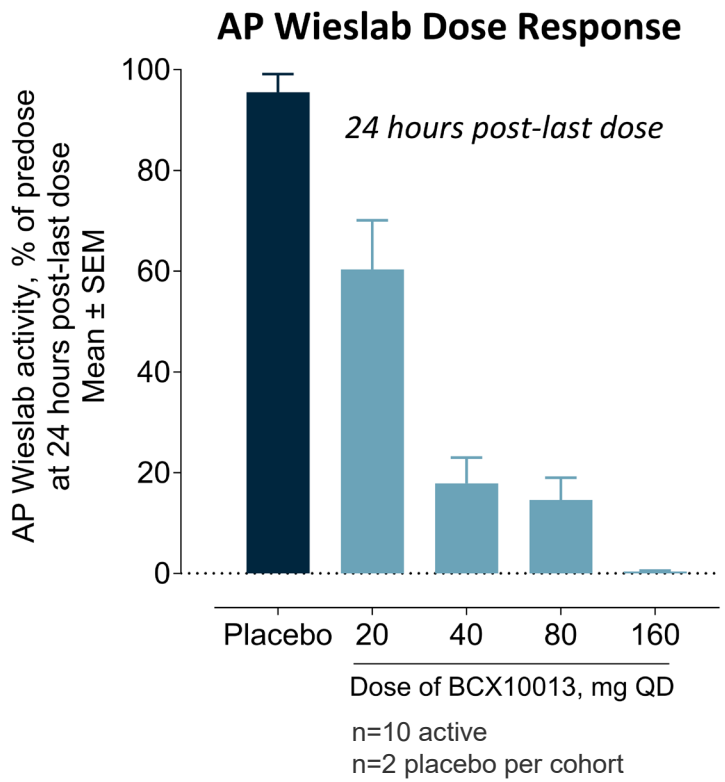
Structure of Human Factor D



aHUS, atypical hemolytic uremic syndrome; AP; alternative pathway; C3G, complement 3 glomerulopathy; IgAN, Immunoglobulin A nephropathy; PNH, paroxysmal nocturnal hemoglobinuria. 1. Barratt J, et al. *Front Immunol.* 2021 Sep 9;12:712572. 2. Cheung CK, et al. *J Clin Med.* 2021;10(2493):1-19.

IN PHASE 1 HEALTHY VOLUNTEER MAD STUDY, 160 MG ONCE-DAILY BCX10013 SHOWED COMPLETE SUPPRESSION* OF AP





Generally safe and well tolerated in healthy volunteers.
No safety signals have been identified in humans to date.

*On day 14, approximately 96% suppression pre-dose and 99% suppression 24 hours post-dose.
AP, alternative pathway; MAD, multiple ascending dose; MG, milligram; QD, once daily. BioCryst Pharmaceuticals data on file 2023.

WE ARE NOW EVALUATING BCX10013, A POTENTIAL BEST-IN-CLASS ONCE-DAILY ORAL, IN A PNH STUDY WITH STRICT SUCCESS CRITERIA

An open-label, Phase 1b intra-subject dose-escalation study evaluating safety and tolerability of BCX10013 in up to 15 adults with PNH **has started dosing.**

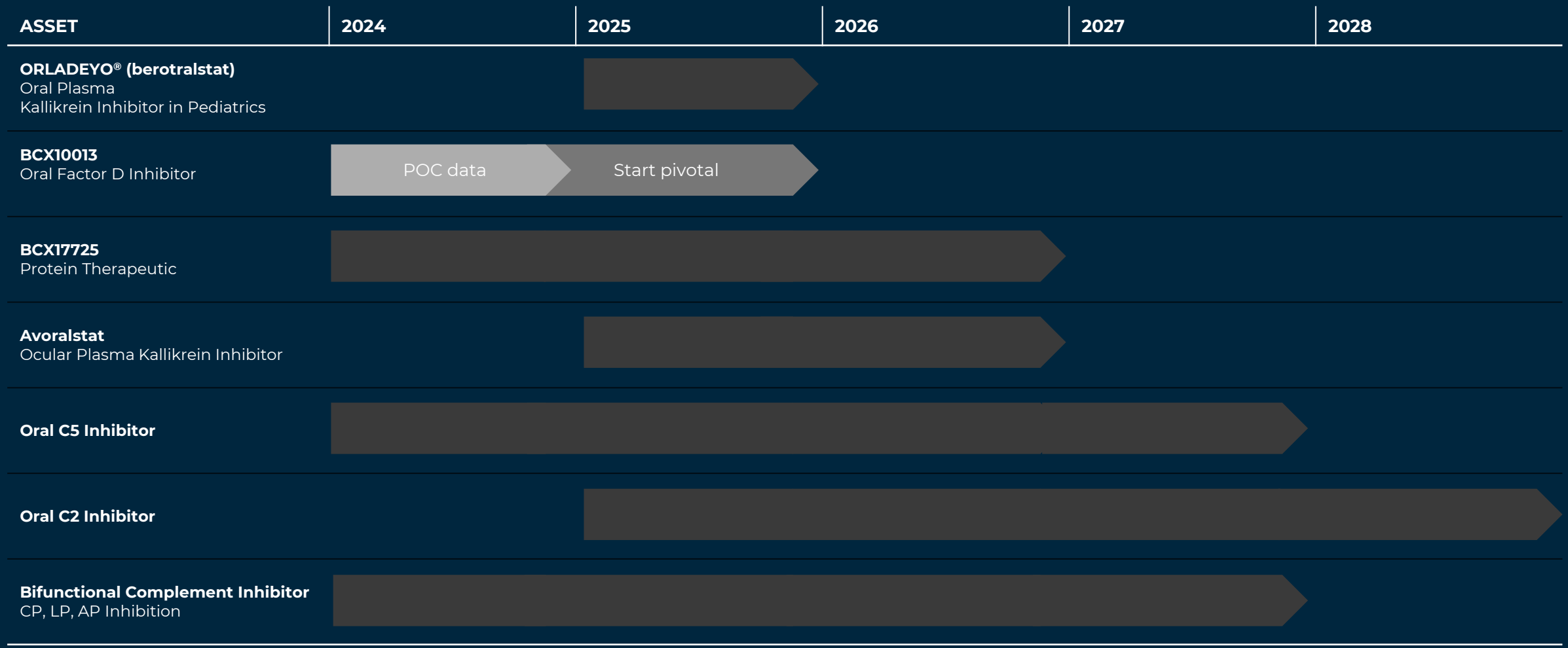
Dosing of BCX10013 is **once daily**, with dose increased in steps to achieve optimum control of disease.

Efficacy goal
Control of hemolysis similar to that reported for iptacopan with LDH < 1.5 x ULN.

Safety goals
Safe and generally well tolerated with once-daily chronic dosing at dosages meeting efficacy goal.

LDH, lactate dehydrogenase; PNH, paroxysmal nocturnal hemoglobinuria; ULN, upper limit normal.

PIPELINE PROGRAM MILESTONES



AP, alternative pathway; C2, complement component 2; C5, complement component 5;
CP, classical pathway; LP, lectin pathway; POC, proof of concept; sNDA, supplemental new drug application.

FIRST-IN-CLASS BIFUNCTIONAL COMPLEMENT INHIBITOR TARGETS CP, LP AND AP

OUR BROAD AND DIVERSIFIED 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 in Pediatrics	**Hereditary Angioedema (HAE)**					
BCX10013 Oral Factor D Inhibitor	**Complement-Mediated Diseases**					
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 CP, LP, AP Inhibition	**Complement-Mediated Diseases**					

*Typically Phase 1-2 studies.
†Typically Phase 3 studies.
C5, complement component 5; C2, complement component 2; CP, classical pathway; LP, lectin pathway, AP, alternative pathway.

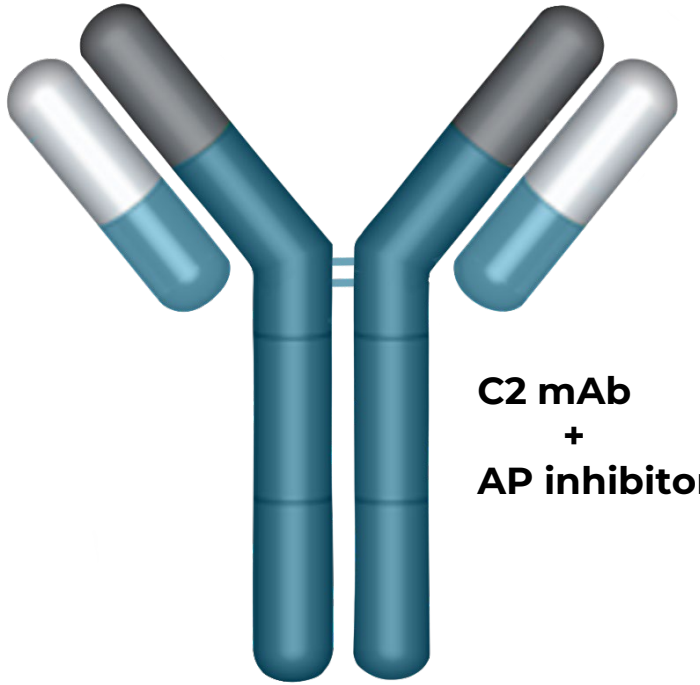
THE BIFUNCTIONAL INHIBITOR PROJECT COMBINES ANTI-C2 MAB WITH AP INHIBITOR IN ONE MOLECULE

Many serious disorders are driven by **activation of multiple complement pathways.**[1]

C2 activation leads to the production of C3 and C5 convertases of the classical and lectin complement pathways.[2]

The Alternative Pathway amplifies both CP- and LP-driven complement cascades.[2]

Bifunctional inhibitor project **targets C2 and AP inhibition in the same molecule.**



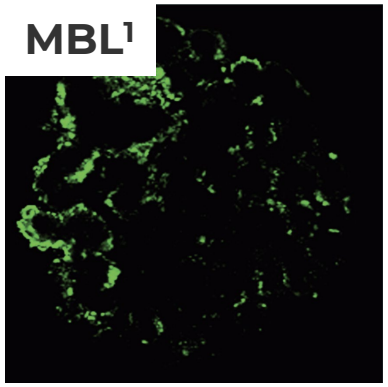
AP, alternative pathway; C2, complement component 2; C3, complement component 3; C5, complement component 5; CP; classical pathway; LP; lectin pathway; mAb, monoclonal antibody. 1. Barratt J, et al. *Front Immunol.* 2021 Sep 9;12:712572. 2. Dunkelberger JR, et al. *Cell Research*. 2010;20:34-50.

SERIOUS DISEASES WITH PATHOLOGIC ACTIVATION OF MULTIPLE COMPLEMENT PATHWAYS*

Lupus Nephritis

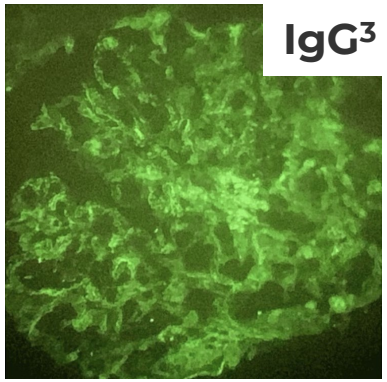
LP

MBL[1]



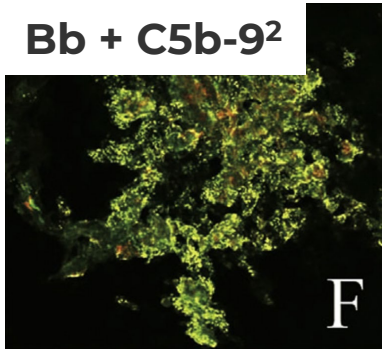
CP

IgG[3]



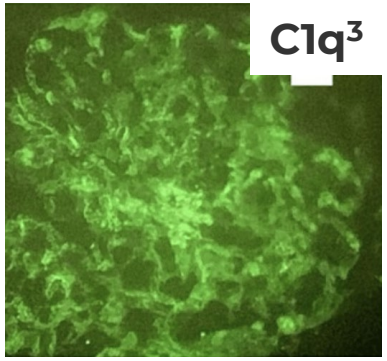
AP

Bb + C5b-9[2]



CP

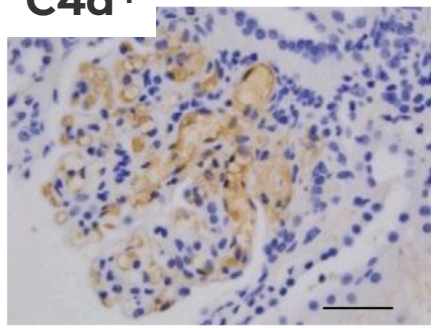
C1q[3]



Progressive IgA Nephropathy

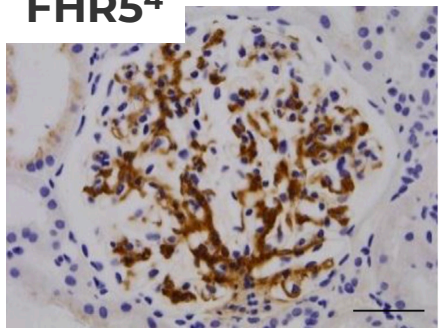
LP

C4d[4]



AP

FHR5[4]



*Examples. Ab, antibody; AP, alternative pathway; Bb, activated factor B; C1q, complement component 1q; C3d, complement component 3d; C4d, complement component 4d; C5b-9, complement component 5b-9; CP, classical pathway; FHR5, factor H-related protein 5; IgG, immunoglobulin G; LP, lectin pathway; MBL, mannose binding lectin.

1. Sato N, et al. *Lupus*. 2011;20(13):1378-1386. 2. Song D, et al. *Am J Medical Sci*. 2017;353(3):247-257. 3. Javeed S, et al. *Cureus*. 2022;14(5)e25363. 4. Medjeral-Thomas NR, et al. *Kidney Int Reports*. 2018;3(2):426-438.

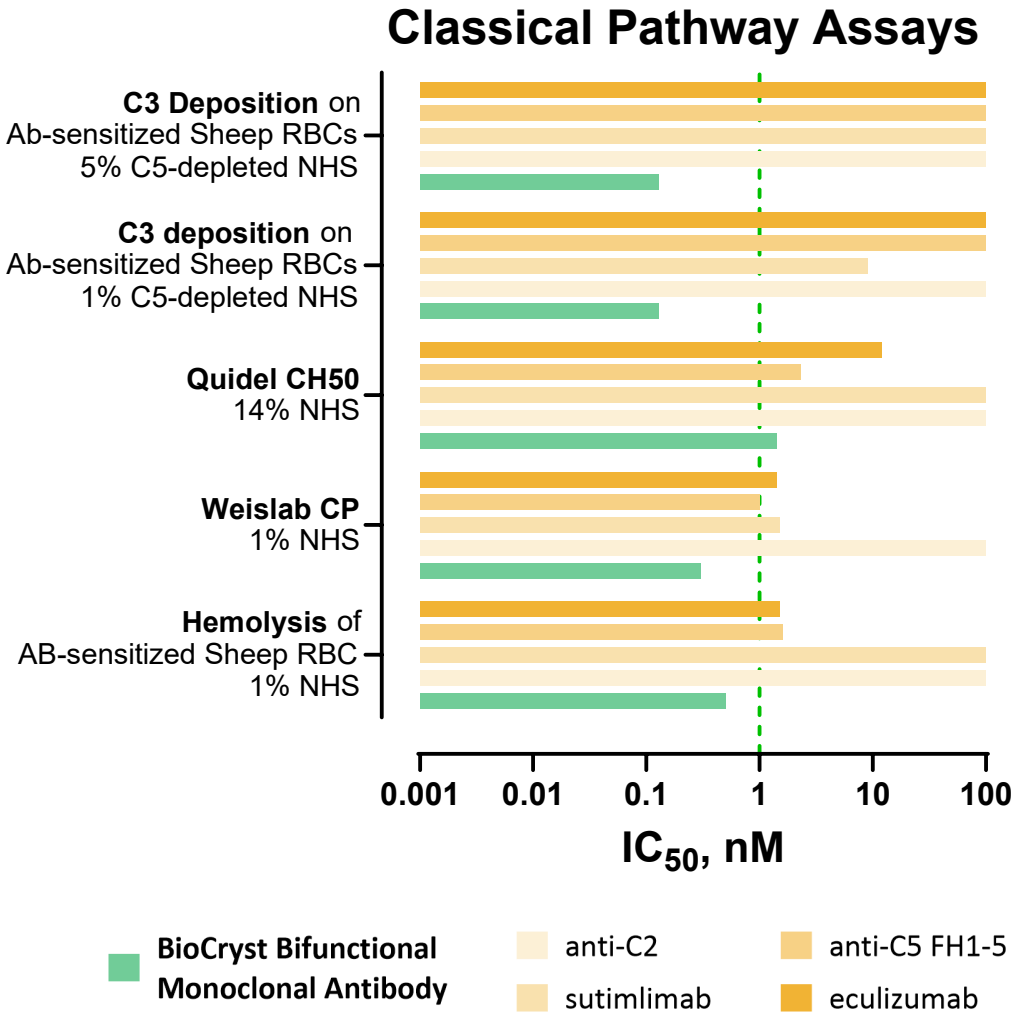
POTENT INHIBITION OF THE CLASSICAL PATHWAY*

5 assays evaluating the Classical Pathway of complement

Assays measure 3 critical complement effector functions: **C3 opsonization, C5b-9 (MAC) formation, and cell lysis**

Low nM or sub-nM potency across each CP assay

More potent than:
- Eculizumab
- Sutimlimab
- Anti-C5 FH1-5 bifunctional Ab
- Anti-C2 Ab



*Representative example
Ab, antibody; AP, alternative pathway; C2, complement component 2; C3, complement component 3; C5, complement component 5; C5b-9, complement component 5b-9; CAD, cold agglutinin disease; CP, classical pathway; FH1-5, factor H 1-5; IC_{50}, half maximum inhibitor concentration; LP, lectin pathway; MAC, membrane attack complex; NHS, normal human serum; nM, nanomolar; RBC, red blood cell. BioCryst Pharmaceuticals data on file 2023.

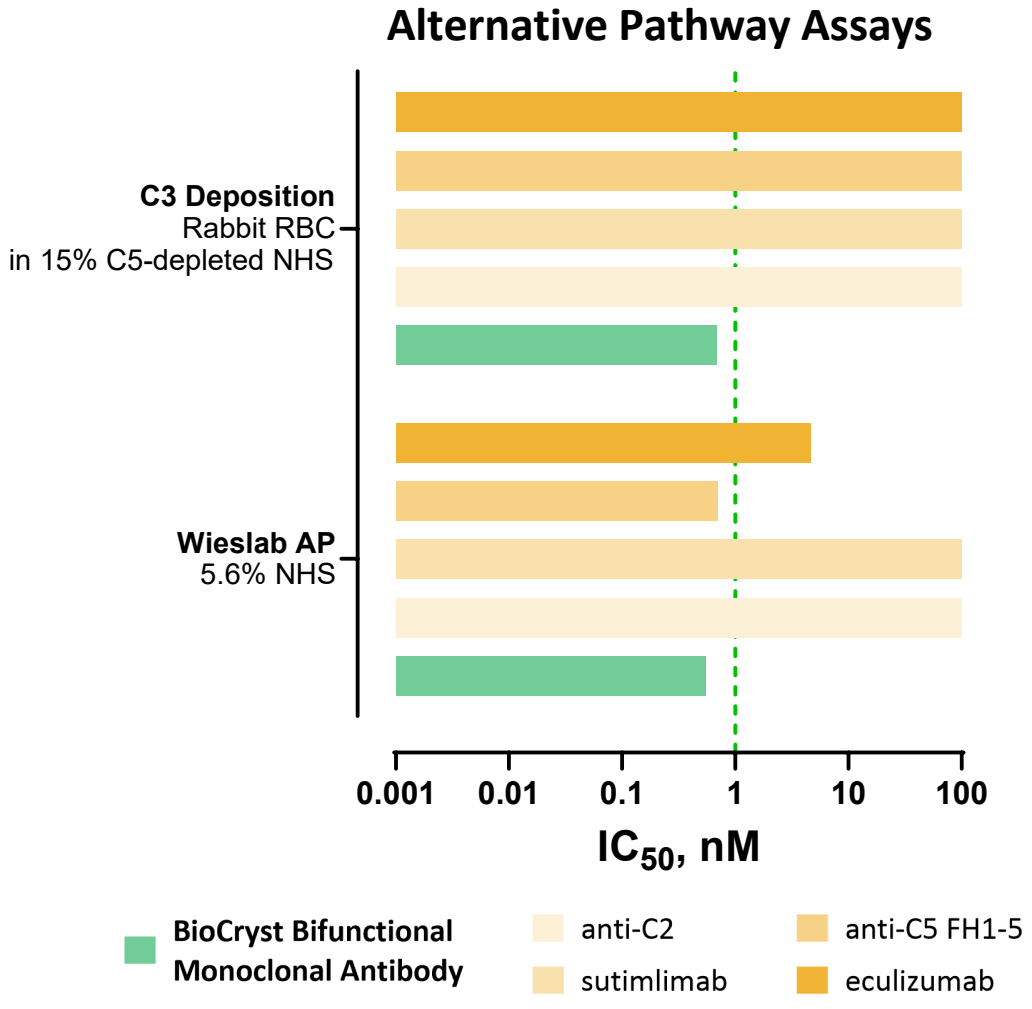
POTENT INHIBITION OF THE ALTERNATIVE PATHWAY*

2 different assays evaluating the Alternative Pathway of complement

Assays measure 2 critical complement effector functions: **C3 opsonization and C5b-9 (MAC) formation**

Sub-nM potency in both alternative pathway (AP) assays

More potent than:
- Eculizumab
- Sutimlimab
- Anti-C5 FH1-5 bifunctional Ab
- Anti-C2 Ab



*Representative example
Ab, antibody; AP, alternative pathway; C2, complement component 2; C3, complement component 3; C5, complement component 5; C5b-9, complement component 5b-9; CP, classical pathway; FH1-5, factor H 1-5; IC_{50}, half maximum inhibitor concentration; LP, lectin pathway; NHS, normal human serum; nM, nanomolar; RBC, red blood cell. BioCryst Pharmaceuticals data on file 2023.

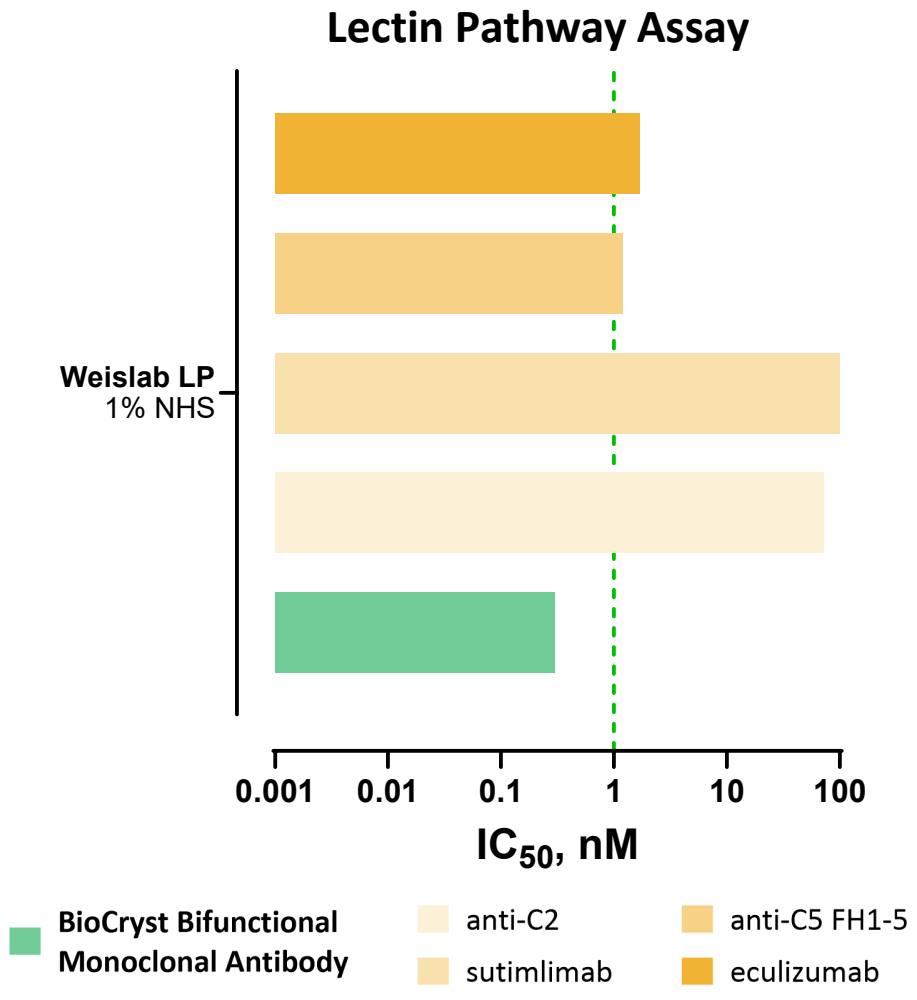
POTENT INHIBITION OF THE LECTIN PATHWAY*

Commercial assay evaluating the Lectin Pathway of complement

Assay measures critical complement effector function: **C5b-9 (MAC) formation**

Sub-nM potency

More potent than:
- Eculizumab
- Sutimlimab
- Anti-C5 FH1-5 bifunctional Ab
- Anti-C2 Ab



*Representative example
Ab, antibody; C2, complement component 2; C5, complement component 5; C5b-9, complement component 5b-9; FH1-5, factor H 1-5; IC_{50}, half maximum inhibitor concentration; LP, lectin pathway; MAC, membrane attack complex; NHS, normal human serum; nM, nanomolar; RBC, red blood cell. BioCryst Pharmaceuticals data on file 2023.

POTENT INHIBITION OF RED BLOOD CELL OPSONIZATION IN COLD AGGLUTININ DISEASE PATIENT SAMPLE*

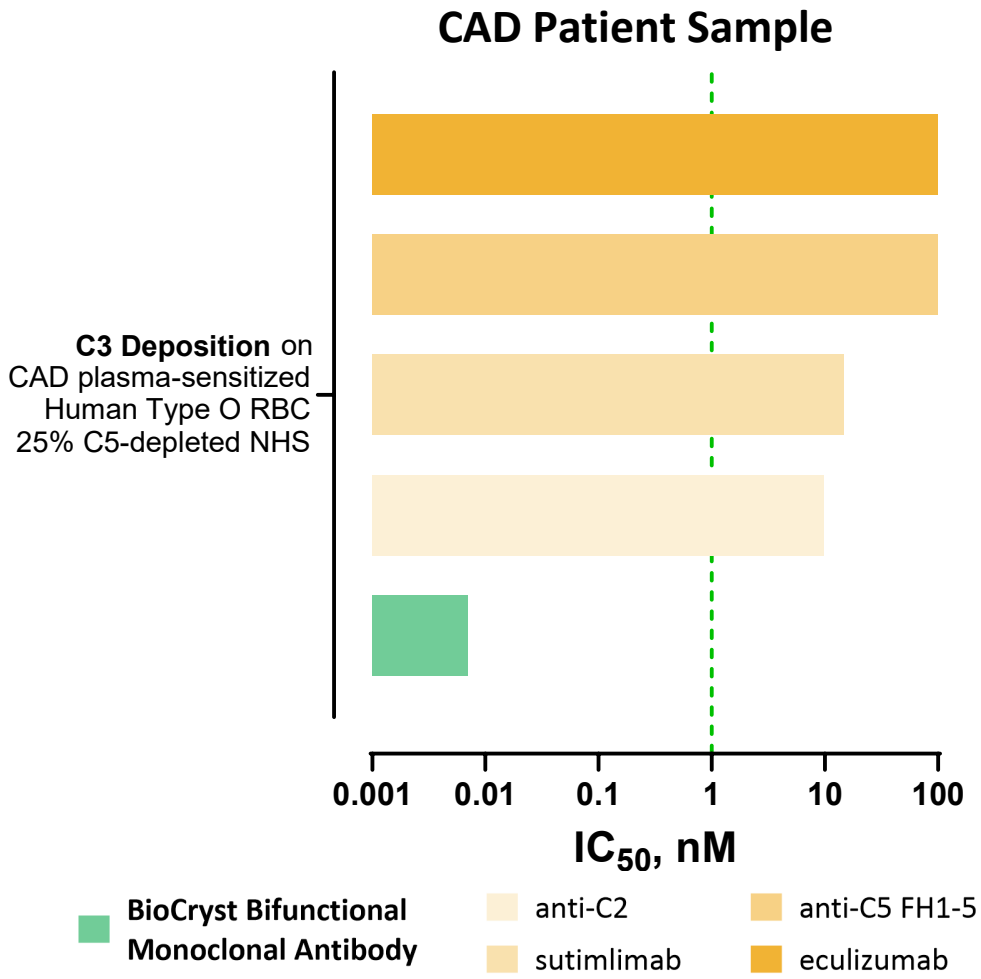
In CAD, the IgM antibodies bind to RBCs and activate complement. This assay directly tests a **CAD patient sample**

The assay measures the critical pathologic step in CAD: **C3 opsonization**

Picomolar range potency

>1,000 fold more potent than:

- Eculizumab
- Sutimlimab (approved to treat CAD)
- Anti-C5 FH1-5 bifunctional Ab
- Anti-C2-CCP2 Ab



*Representative example
Ab, antibody; C3, complement component 3; C5, complement component 5; C5b-9, complement component 5b-9; CAD, cold agglutinin disease;; FH1-5, factor H 1-5; IC_{50}, half maximum inhibitor concentration; IgM, immunoglobulin M; NHS, normal human serum; nM, nanomolar; RBC, red blood cell. BioCryst Pharmaceuticals data on file 2023.

BIFUNCTIONAL COMPLEMENT INHIBITOR BLOCKS MULTIPLE COMPLEMENT PATHWAYS*

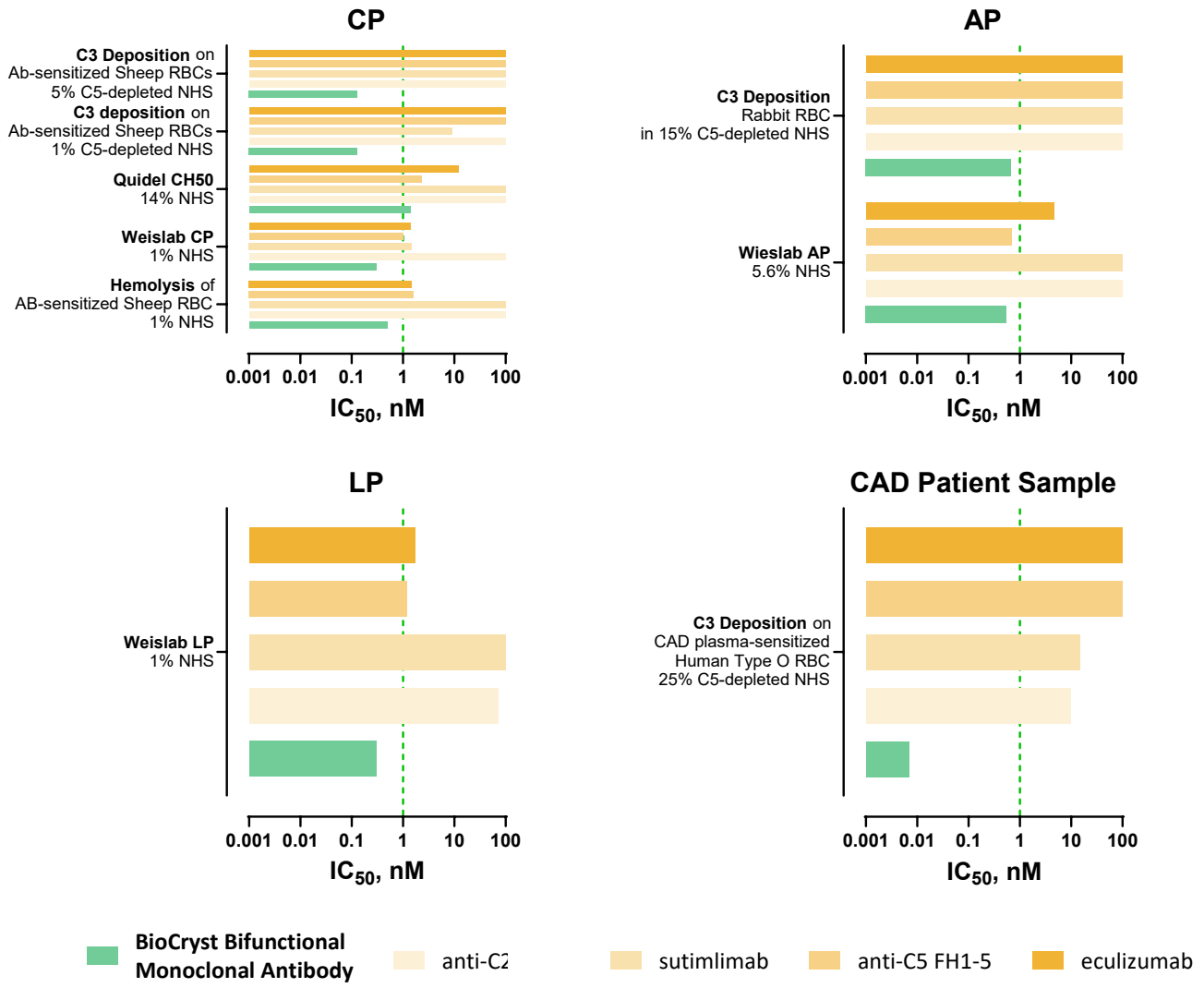
9 different assays evaluating CP, LP, AP, and combined CP+AP of complement

Assays measure critical complement effector functions: **C3 opsonization, C5b-9 (MAC) formation, and cell lysis**

Low nM or sub-nM potency across different assays of CP, AP and LP

More potent than:

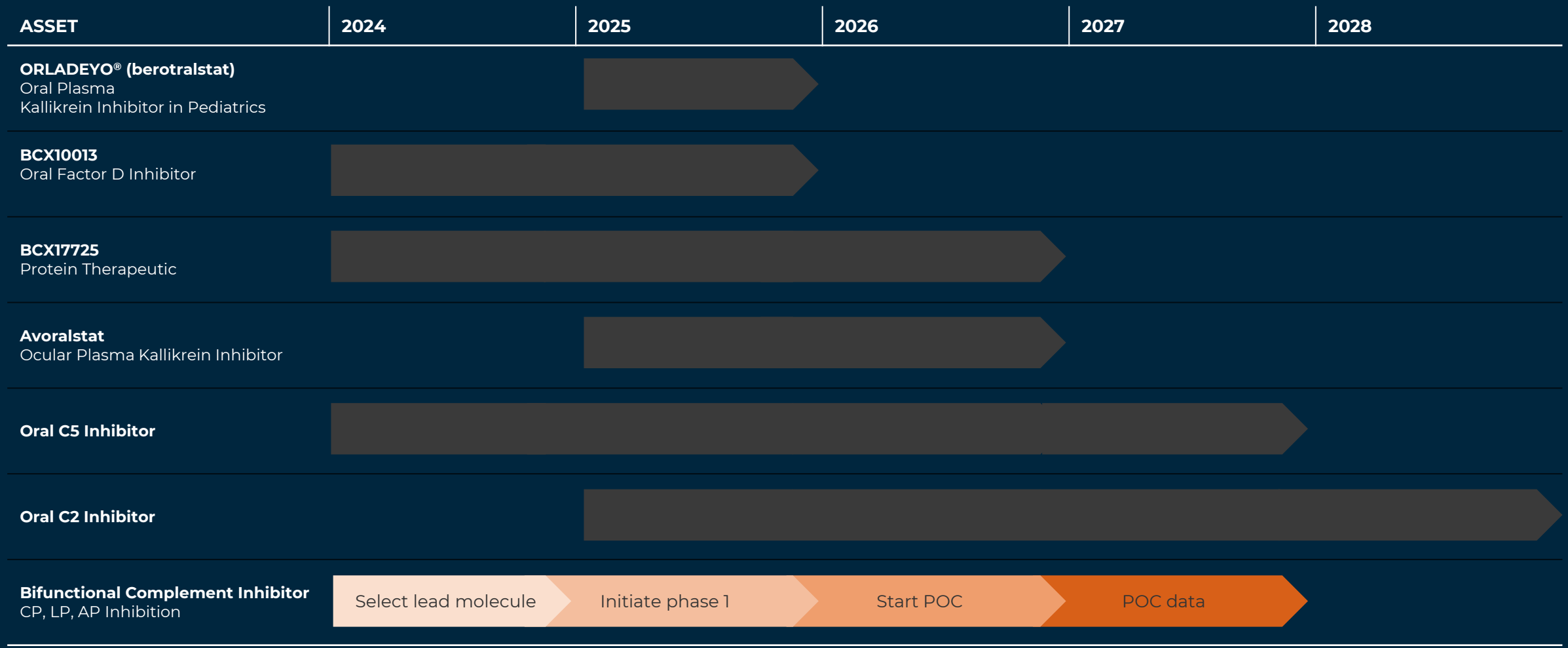
- Eculizumab
- Sutimlimab
- Anti-C5 FH1-5 bifunctional Ab
- Anti-C2 Ab



*Representative example

Ab, antibody; AP, alternative pathway; C2, complement component 2; C3, complement component 3; C5, complement component 5; C5b-9, complement component 5b-9; CAD, cold agglutinin disease; CP, classical pathway; FH1-5, factor H 1-5; IC_{50}, half maximum inhibitor concentration; LP, lectin pathway; MAC, membrane attack complex; NHS, normal human serum; nM, nanomolar; RBC, red blood cell. BioCryst Pharmaceuticals data on file 2023.

PIPELINE PROGRAM MILESTONES



AP, alternative pathway; C2, complement component 2; C5, complement component 5;
CP, classical pathway; LP, lectin pathway; POC, proof of concept; sNDA, supplemental new drug application.

BCX17725: A NOVEL PROTEIN THERAPY FOR NETHERTON SYNDROME

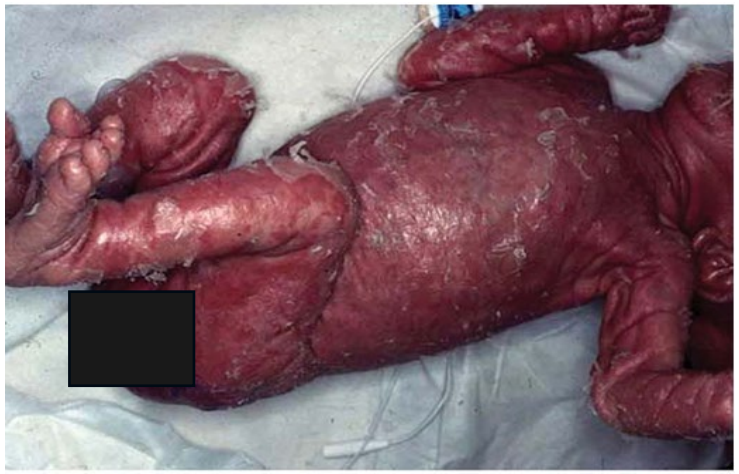
Dr. Ryan Arnold, Chief Medical Officer

OUR BROAD AND DIVERSIFIED 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 in Pediatrics	**Hereditary Angioedema (HAE)**					
BCX10013 Oral Factor D Inhibitor	**Complement-Mediated Diseases**					
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 CP, LP, AP Inhibition	**Complement-Mediated Diseases**					

*Typically Phase 1-2 studies.
†Typically Phase 3 studies.
C5, complement component 5; C2, complement component 2; CP, classical pathway; LP, lectin pathway, AP, alternative pathway.

NETHERTON SYNDROME (NS) – A RARE, GENETIC SKIN DISORDER WITH SIGNIFICANT BURDEN



Leclerc-Mercier S, et al. *American Journal of Dermatopathology*. 2016;38(2).

Often presents as ***red, scaly, inflamed skin*** in newborn or infant. Dehydration and infection are common and can be serious.[1]

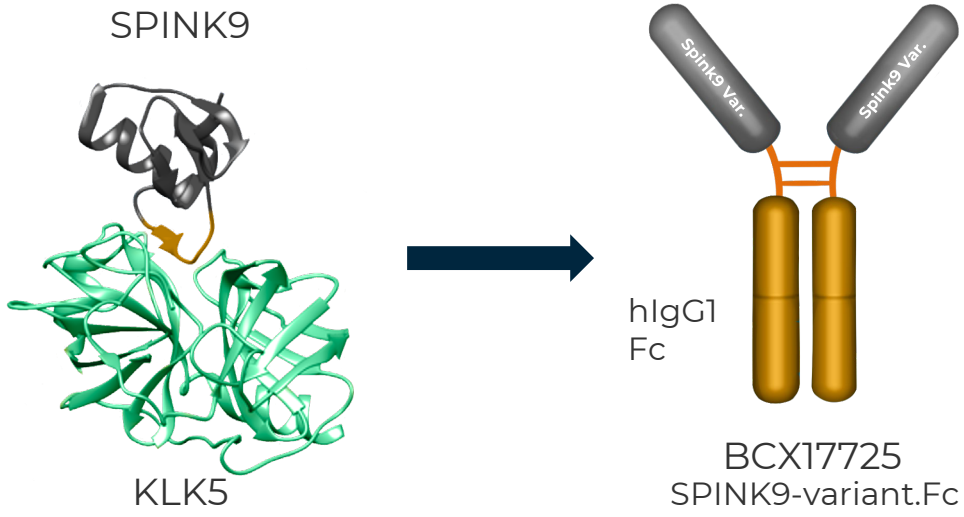
Caused by **deficiency of a natural inhibitor (SPINK5) of KLK5**, a serine protease responsible for regulating skin shedding[2-4]

Excessive KLK cascade activity leads to breakdown of the skin barrier and is associated with various inflammatory skin diseases[5]

There are **no approved treatments** for NS[2,3]

KLK5 inhibition can restore normal skin turnover[2]

BCX17725 is an investigational **potential disease modifying** fusion protein KLK5 inhibitor



KLK, kallikrein; KLK5, kallikrein-related peptidase 5; SPINK5, serine protease inhibitor kazal type 5; SPINK9, serine protease inhibitor kazal type 9.

1. NIH. Netherton syndrome. February 2023. Accessed August 24, 2023. https://rarediseases.info.nih.gov/diseases/7182/netherton-syndrome 2. Furio L, et al. *PLoS Genetics*. 2015;11(9):e1005389. 3. Saleem HMK, et al. *Cureus*. 2018;10(7):e3070. 4. Zani MB, et al. *Frontiers in Medicine*. 2022;8(777619):1-11. 5. Nauroy P, et al. *Matrix Biol Plus*. 2020;1-12.

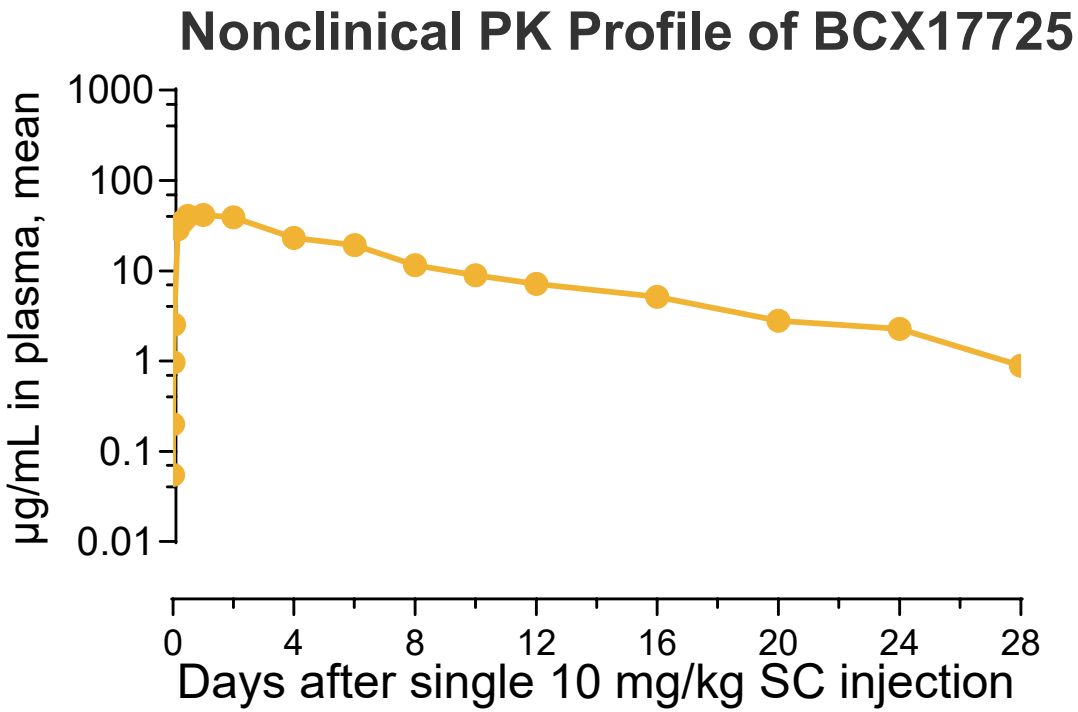
BCX17725 NONCLINICAL CHARACTERIZATION: POTENTIAL FOR BEST-IN-CLASS TARGETED TREATMENT FOR NETHERTON SYNDROME

75% bioavailability after SC injection in NHP, **supporting SC injection administration in the clinic**

Favorable PK in NHP, **compatible with Q2Weeks or longer intervals of administration in the clinic**

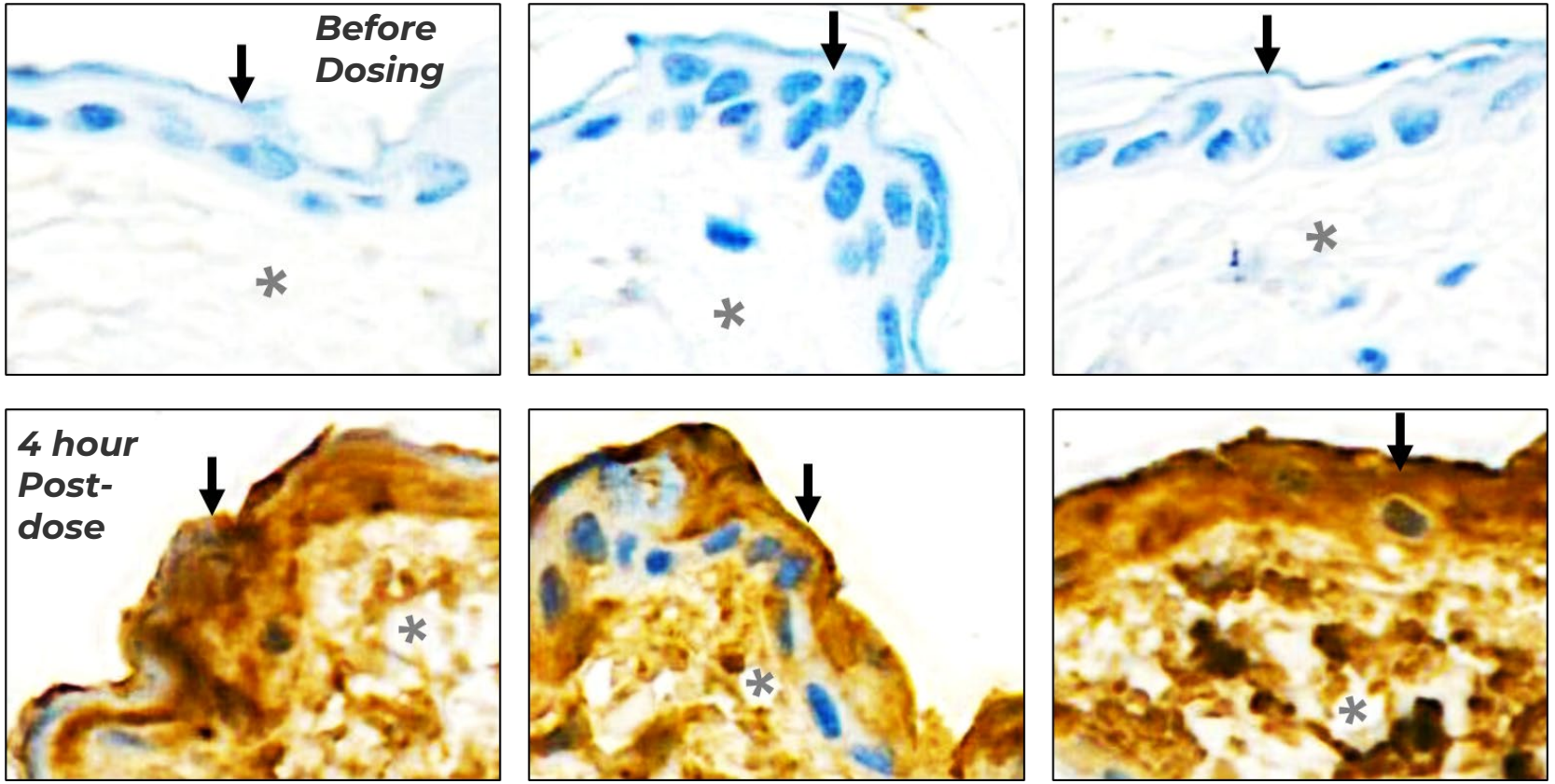
Low in-silico immunogenicity score – lower than unmodified normal human IgG-Fc, predicting **minimal risk of anti-drug antibodies**

More than 10-fold higher potency on KLK5 than DI-50055 SPINK5 Fc fusion protein, **consistent with lower clinical doses**



Fc, fragment crystallizable; IgG-Fc, immunoglobulin G-fragment crystallizable; KLK5, kallikrein-related peptidase 5; NHP, non-human primate; PK, pharmacokinetics; Q2Weeks, once every 2 weeks; SPINK5, serine protease inhibitor kazal type 5; SC, subcutaneous. BioCryst Pharmaceuticals data on file 2023.

BCX17725 PRECLINICAL DATA SHOW RAPID DISTRIBUTION TO EPIDERMIS OF SKIN FOLLOWING IP ADMINISTRATION IN MOUSE



Magnification = 400x

In a nonclinical study, **BCX17725 was dosed by IP injection**

Skin samples were assayed for BCX17725 using a specific antibody and peroxidase reaction – this shows up as **brown with intensity proportional to drug content**

BCX17725 gets to the epidermis, the target tissue required for treating Netherton syndrome

↓ **Epidermal layer**

* Dermis

Wild-type mice were administrated 100 mg/kg BCX17725 (version suitable for murine studies)' IP, intraperitoneal; BioCryst Pharmaceuticals data on file 2023.

PIPELINE PROGRAM MILESTONES

AP, alternative pathway; C2, complement component 2; C5, complement component 5;
CP, classical pathway; LP, lectin pathway; POC, proof of concept; sNDA, supplemental new drug application.

BCX17725: BEST-IN-CLASS COMMERCIAL POTENTIAL

Prevalence

- **Up to 5,000** individuals in the US likely have Netherton syndrome[1] with ~1,600 estimated from claims analysis*

Target Profile

- ≤ 2mL SC injection, every 2 weeks or longer, pediatric and adult

Commercial Opportunities

- Best-in-class dosing and efficacy
- Patient diagnosis/market expansion
- Ultra-rare disease pricing potential
- Indication expansion

Competitor	MoA	Dosing / Administration	Development Stage	How BCX17725 Likely to be Best-in-Class
QRX003 (Quoin)	Broad spectrum serine protease inhibitor	Topical	Phase 2/3	• Lower treatment burden • Improved bioavailability with systemic delivery, leading to better efficacy
DS2325a (Daiichi Sankyo)	KLK5 inhibitor	Weekly SC (600mg)	Phase 1/2	• Lower dose, smaller volume, less frequent dosing
Spesolimab (Boehringer)	IL36 inhibitor	Monthly IV	Phase 2/3	• Better efficacy based on KLK5 target • Self-administered dosing

*BioCryst Pharmaceuticals Data on file estimation based on US claims analysis.
IL36, interleukin-36; IV, intravenous; KLK5, kallikrein-related peptidase 5; SC, subcutaneous.
1. NIH. Netherton syndrome. February 2023. Accessed August 24, 2023. https://rarediseases.info.nih.gov/diseases/7182/netherton-syndrome

KEY TAKEAWAYS: BCX17725 FOR NETHERTON SYNDROME

- Netherton syndrome is a serious ultra-rare disease caused by loss of function mutations of a natural KLK5 inhibitor
- There are no approved treatments for Netherton syndrome
- BCX17725 is an Fc fusion bioengineered natural human inhibitor of KLK5
- Favorable nonclinical profile of BCX17725 supports potential for best-in-class profile
- We aim to deliver POC results in Netherton syndrome in 2026

Fc, fragment crystallizable; KLK5, kallikrein-related peptidase 5; PK, pharmacokinetics; POC, proof of concept.

AVORALSTAT
FOR DIABETIC MACULAR EDEMA (DME)

OUR BROAD AND DIVERSIFIED PIPELINE

ASSET	PROGRAM	LEAD OPTIMIZATION	PRE-CLINICAL	PROOF OF CONCEPT*	PIVOTAL†	APPROVED / COMMERCIAL
ORLADEYO® (berotralstat) Oral Plasma Kallikrein Inhibitor	**Hereditary Angioedema (HAE)**					
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BCX10013 Oral Factor D Inhibitor	**Complement-Mediated Diseases**					
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*Typically Phase 1-2 studies.
†Typically Phase 3 studies.
C5, complement component 5; C2, complement component 2; CP, classical pathway; LP, lectin pathway, AP, alternative pathway.

TARGETING PLASMA KALLIKREIN AS AN OPTION TO IMPROVE VISION IN PATIENTS WITH DIABETIC MACULAR EDEMA (DME)

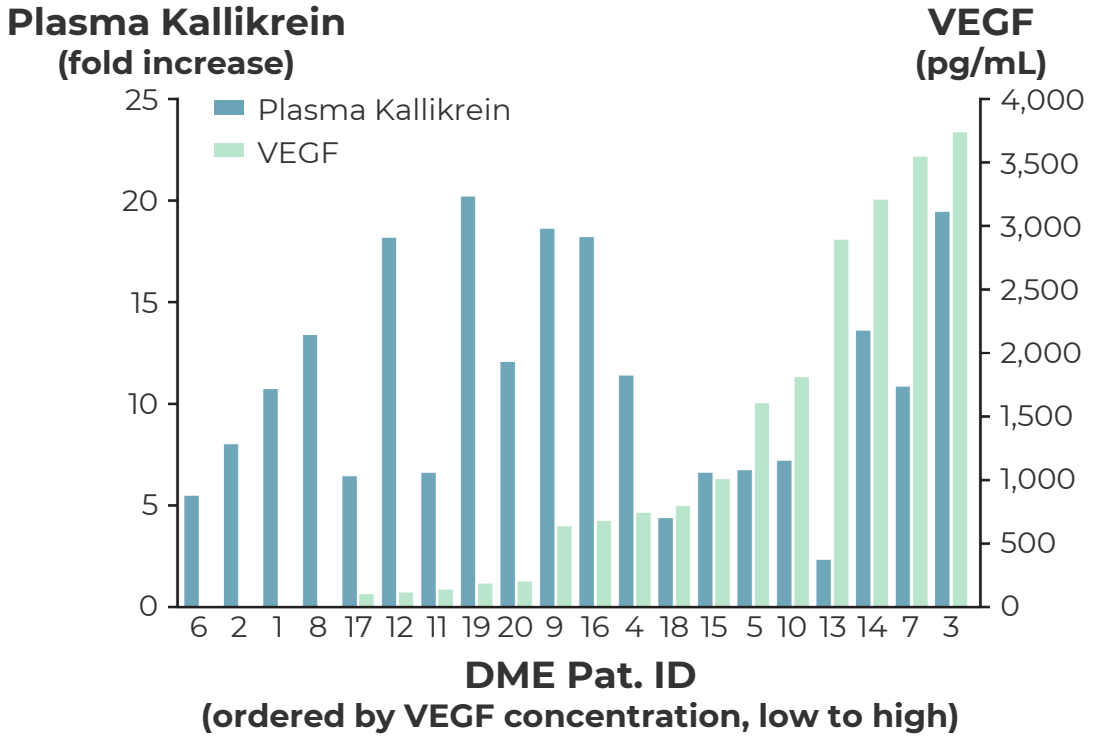
DME **continues to be most common cause of vision loss** in individuals with diabetes[1]

32%-66%

of patients have persistent DME despite anti-VEGF therapies[2]

Plasma kallikrein may be a significant contributor to retinal edema and dysfunction in DME, **independent of VEGF mechanisms**[3]

Analysis of VEGF and Plasma Kallikrein in Human DME Vitreous



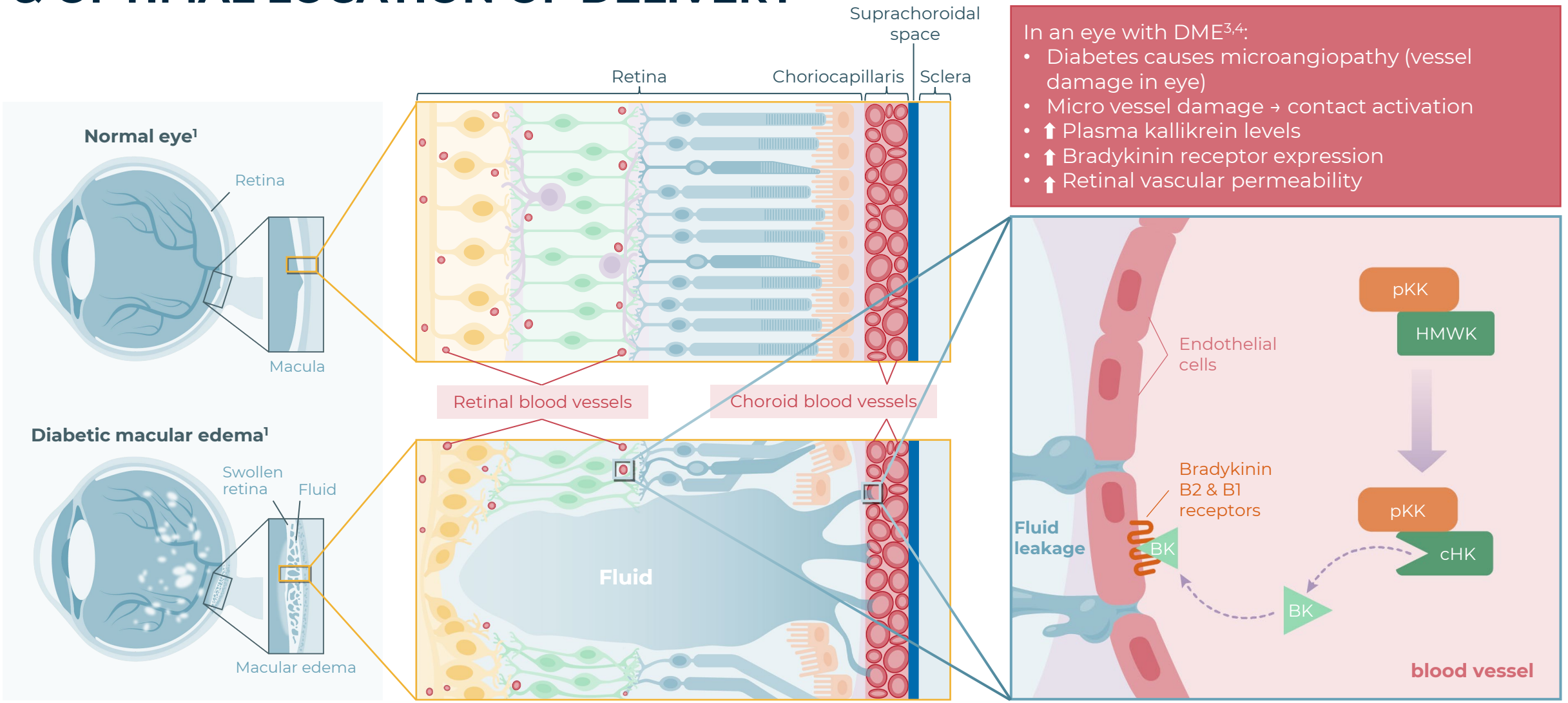
Immunoassays of DME vitreous samples[4]

pg, picograms; mL, milliliter; SoC, standard of care; VEGF, vascular endothelial growth factor.

1. Lee R, et al. *Eye Vis (Lond).* 2015;2:17. 2. Bressler NM, et al. *JAMA Ophthalmol.* 2018;136(3):257-269. 3. Bhatwadekar AD, et al. *Expert Opin Investig Drugs.* 2020;29(3):237-244. 4. Kita T, et al. Diabetes. 2015;64(10):3588-3599.

THE IMPORTANCE OF THE RIGHT DRUG, THE RIGHT MECHANISM, & OPTIMAL LOCATION OF DELIVERY

In an eye with DME[3,4]:
- Diabetes causes microangiopathy (vessel damage in eye)
- Micro vessel damage → contact activation
- ⬆ Plasma kallikrein levels
- ⬆ Bradykinin receptor expression
- ⬆ Retinal vascular permeability



BK, bradykinin; cHK, cleaved high molecular weight kininogen; HMWK, high molecular weight kininogen; pKK, plasma kallikrein

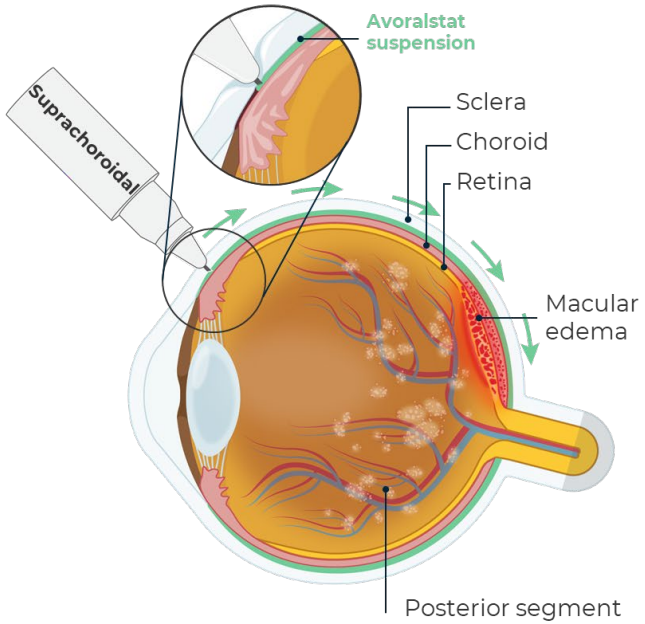
1. Trinh HM, et al. *World J Pharmacol.* 2016;5(1):1-14. 2. Yang S, et al. *Front. Pharmacol.* 2021;12:727870. 3. Kita T, et al. *Diabetes.* 2015;64(10):3588-3599. 4. Lang GE, et al. *TVST.* 2020;9(4)1-12. v.

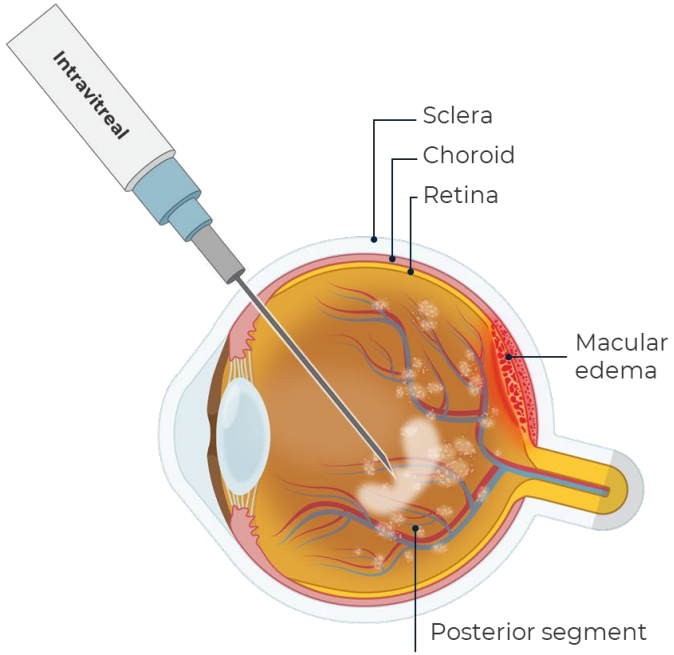
SUPRACHOROIDAL ADMINISTRATION OFFERS SEVERAL ADVANTAGES FOR DELIVERING AVORALSTAT TO TARGET TISSUES IN DME

Potential Advantages

- ✓ Provides targeted delivery of drug into a natural depot reservoir
- ✓ Establishes gradient for drug suspension to slowly release into retina, RPE & choroid
- ✓ Minimizes potential adverse events, such as vitreous hemorrhage

Suprachoroidal injector*



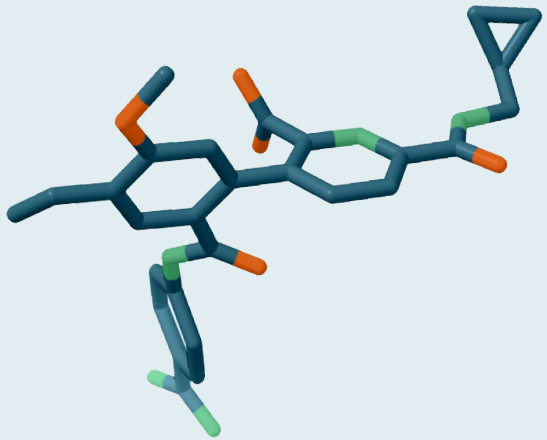


*SCS Microinjector® is licensed from Clearside Biomedical, Inc. RPE, retinal pigment epithelium; SCS, suprachoroidal space.

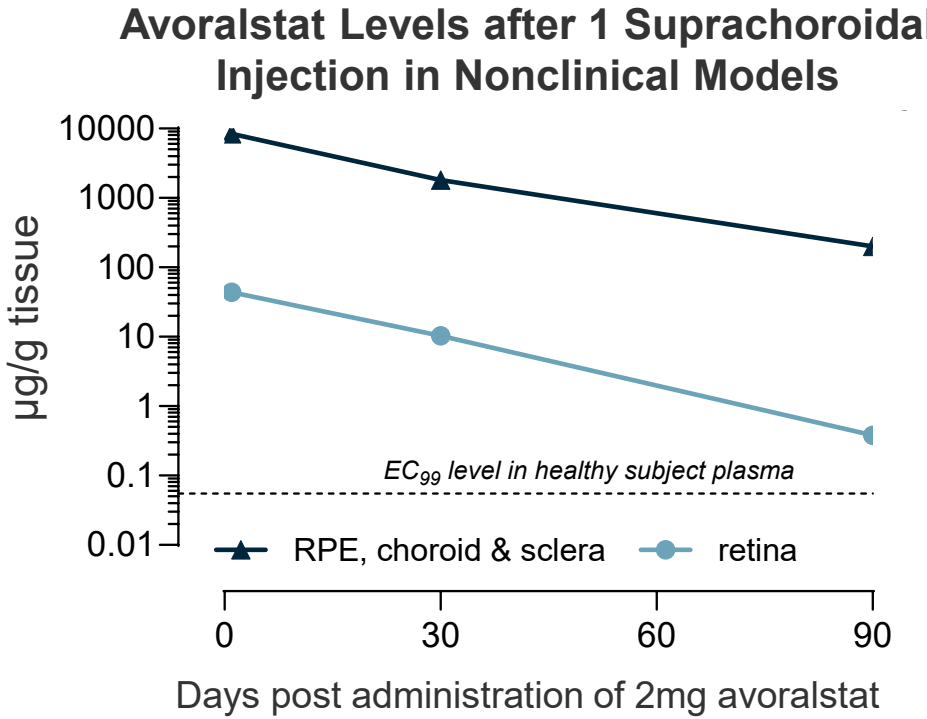
AVORALSTAT: AN OCULAR PLASMA KALLIKREIN INHIBITOR

Oral administration of avoralstat was **safe and well tolerated** in 98 individuals living with HAE and 178 healthy individuals

The AE profile of avoralstat was similar to placebo in a randomized controlled trial[1]



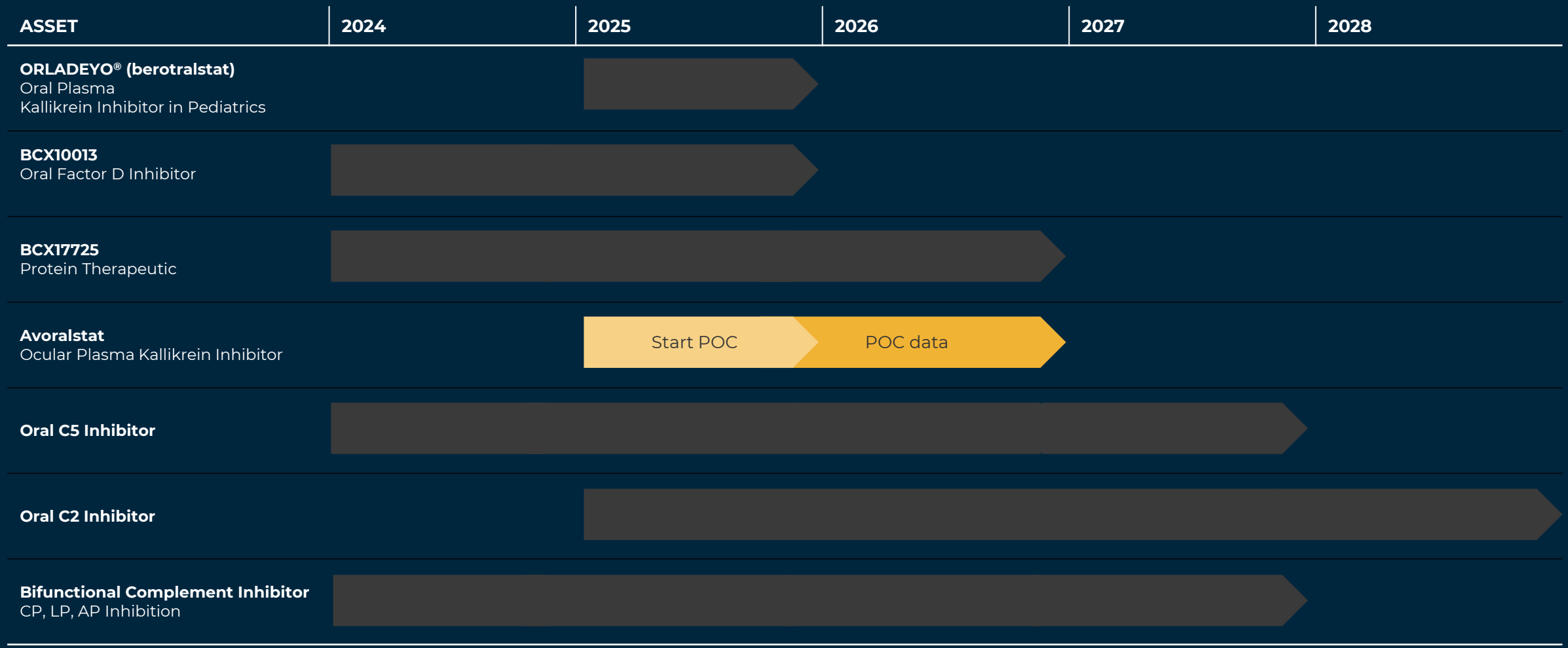
The **low solubility of avoralstat** supports evaluation of a suspension depot formulation for ophthalmic injection



High levels of avoralstat are maintained for at least 90 days in nonclinical study of suprachoroidal injection[2]

AE, adverse effects; HAE, hereditary angioedema; RPE, retinal pigment epithelium.
1. Riedl MA, et al. *Allergy*. 2018;73(9):1871-1880. 2. BioCryst Pharmaceuticals data on file 2023.

PIPELINE PROGRAM MILESTONES



AP, alternative pathway; C2, complement component 2; C5, complement component 5;
CP, classical pathway; LP, lectin pathway; POC, proof of concept; sNDA, supplemental new drug application.

AVORALSTAT COULD MEET THE NEED FOR AN EFFECTIVE SECOND-LINE THERAPY

Target Profile: Suprachoroidal injections every 3 months or better, with BCVA improvement (mean ≥ 6 letters) in patients with suboptimal response to VEGF inhibitors

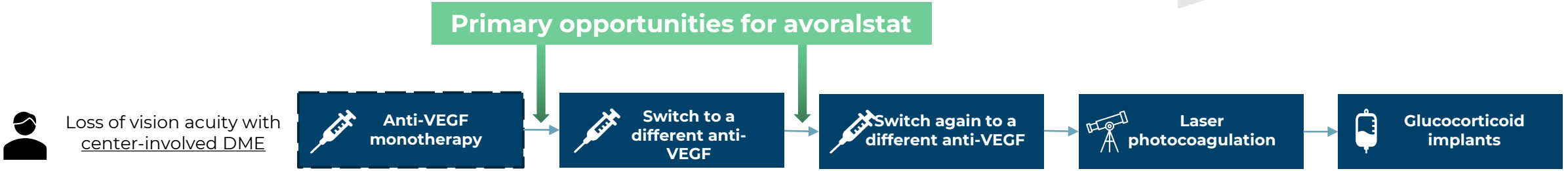
- Anti-VEGF therapies are the backbone of DME treatment and require intravitreal injections every 1 to 4 months[1,2]
- Current guidelines recommend up to 3 attempts at anti-VEGF therapy, with off-label Avastin (bevacizumab), Eylea (aflibercept), and Lucentis (ranibizumab) being the top 3 recommended agents
- The American Academy of Ophthalmology (AAO) estimates that **anti-VEGF therapy is unsuccessful or inadequate in 40% of patients with DME[3]**

"The MOA is not what we know, it's a kallikrein inhibitor. That's good, we don't need another anti-VEGF inhibitor, we need something in another pathway."

– Diabetic Macular Edema KOL[4]

"Any new MOA is exciting to me. I love that it is not another recycle of an old anti-VEGF. We have been swirling around different ways to make different anti-VEGFs and we need more options."

– Diabetic Macular Edema KOL[4]



BVCA, best-corrected visual acuity; DME, diabetic macular edema; MOA, mechanism of action; VEGF, vascular endothelial growth factor.
1. McFadden E., Decision Resources Group, 2018. 2. Diabetic Macular Edema- Epidemiology Forecast to 2032, 2018. 3. Elyasi N, et al. *EyeNet Magazine*. 2021;35-37. 4. BioCryst Pharmaceuticals Market Research Q2 2023.

DME IS A LARGE POPULATION BUT TREATMENTS ARE DELIVERED BY A SMALL NUMBER OF SPECIALISTS, COMPATIBLE WITH A RARE DISEASE

DME PROGRESSION[1-5]

Type I Diabetes — **~3.7M US Patients**

~75% Type I patients develop diabetic retinopathy

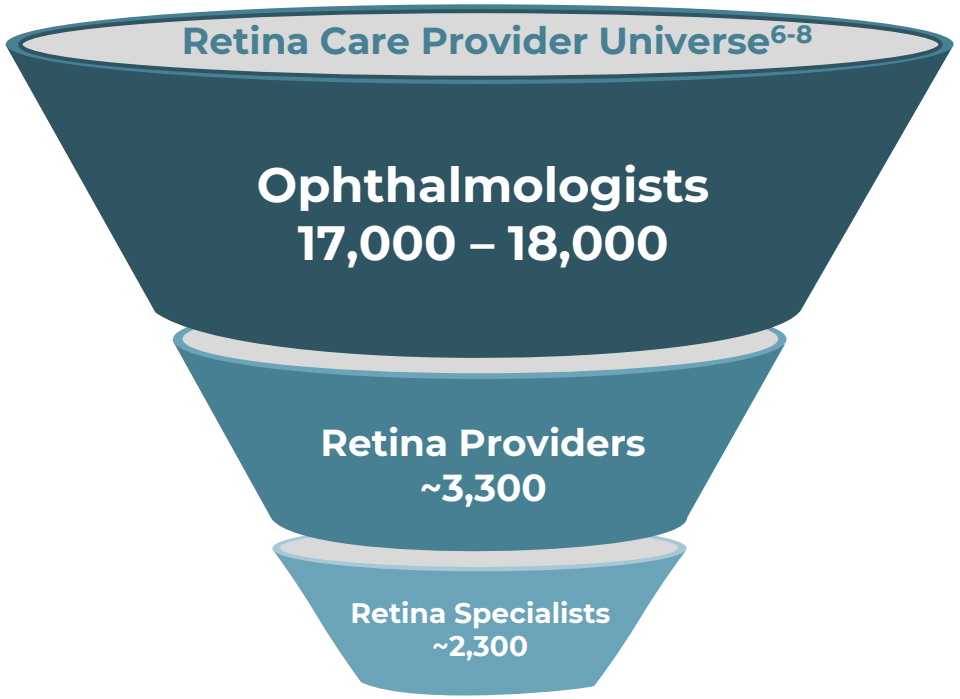
Type II Diabetes — **~33.3M US Patients**

>25% Type II patients develop diabetic retinopathy

Diabetic Retinopathy — **~11M US Patients**

~10-17% of patients with diabetic retinopathy develop DME

Diabetic Macular Edema — **~1.5M US Patients**



BioCryst has called on **nearly 4,000** US physicians in 2023 alone for ORLADEYO

DME, diabetic macular edema; 1. BioMedTracker, Accessed August 2023; Prevent Blindness: Bringing Americans to Eye Care. 2. McFadden E., Decision Resources Group, 2018. 3. Diabetic Macular Edema - Epidemiology Forecast to 2032, 2022. 4. National Diabetes Education Program; BioMedTracker. 5. Romero-Aroca P. Managing diabetic macular edema: The leading cause of diabetes blindness. World J Diabetes. 2011, accessed August 2023. 6. Healio "Access to Retina Providers Shows no Geographic Bias" (March 2019). 7. AAO "Facts and Figures" (Jan 2020). 8. Pandit, et al. IOVS, 2020.

AVORALSTAT HAS POTENTIAL TO BE LEADING SECOND-LINE THERAPY IN A GROWING DME MARKET

$2B US VEGF inhibitor sales in 2022 expected to grow to $4B by 2028, driven by expanded patient identification and treatment[1]

Competitor[2]	MoA[2]	Dosing/Administration[2]	Development Stage	How Avoralstat Will be Best-in-Class
Avastin, Eyelea, Lucentis, Vabysmo, Beovu	VEGF inh	 Intravitreal injections every 1-4 months	Approved	• Head-to-head superiority data vs VEGF inh inadequate responders
Illuvien®, Ozurdex®	Gluco-corticoids	 Implants every 3 months to 3 years	Approved	• Better safety • Better efficacy
THR-149 (Oxurion)	KKI	 Monthly intravitreal injections	Phase 2	• Less frequent dosing • Potentially superior efficacy based on suprachoroidal delivery
RZ-402 (Rezolute)	KKI	 QD Oral	Phase 2	• Potentially superior efficacy based on suprachoroidal delivery

Inh, inhibitor; KKI, plasma kallikrein inhibitor; QD, once daily; VEGF, vascular endothelial growth factor; 1. Evaluate Pharma. 2. www.clinicaltrials.gov.

KEY TAKEAWAYS: AVORALSTAT FOR DME

- Plasma kallikrein inhibition is a promising approach for DME treatment
- Slow dissolution and high potency of avoralstat are ideal characteristics for local depot delivery
- Clearside partnership allows for suprachoroidal delivery of avoralstat for patients with DME
- Potential to be a leading 2L therapy for DME in a growing market

2L, second-line; DME, diabetic macular edema.

ORLADEYO PEDIATRIC INDICATION

OUR BROAD AND DIVERSIFIED 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 in Pediatrics	**Hereditary Angioedema (HAE)**					
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Avoralstat Ocular Plasma Kallikrein Inhibitor	**Diabetic Macular Edema (DME)**					
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Bifunctional Complement Inhibitor CP, LP, AP Inhibition	**Complement-Mediated Diseases**					

*Typically Phase 1-2 studies.
†Typically Phase 3 studies.
C5, complement component 5; C2, complement component 2; CP, classical pathway; LP, lectin pathway, AP, alternative pathway.

ORLADEYO® CAN ADDRESS UNMET NEED IN CHILDREN WITH HEREDITARY ANGIOEDEMA (HAE)

HAE is a rare, potentially life-threatening, and **lifelong disease that typically begins in childhood**[1]

1 in 10,000 to **1 in 50,000** people affected[2]

2 out of 5 patients have their first attack by **5 years of age**[1]

Children have smaller airway diameters, which can increase risk of fatal laryngeal attacks[3]

There is a desire for oral treatments for children with HAE as injectable therapy can be difficult to sustain over time[1,4]

There are no current targeted oral therapies available for prophylaxis in children < 12 years old[5]

Current Prophylaxis Options for Kids

	TAKHZYRO (ages 2+)[6]*: SC injection	**HAEGARDA (ages 6+)[7]:** SC injection	**CINRYZE (ages 6+)[8]:** IV infusion
	TREATMENT SCHEDULE		
Week 1			
Week 2			
Week 3			
Week 4			

*The dosing frequency in patients aged 2 to <6 years is every 4 weeks, and in patients 6 to 12 years old, every 2 weeks, with every 4 weeks considered in some.
SC, subcutaneous; IV, intravenous.

1. Tachdjian R, et al. *Clin Pediatr (Phila).* 2023;99228231155703. 2. Bernstein JA. *Allergy Asthma Proc.* 2013;34(1):3-6. 3. Betschel SD, et al. *J Allergy Clin Immunol Pract.* 2023;11:2315-25. 4. Wahn V, et al. *Pediatric Allergy and Immunology.* 2020;31:974-989. 5. Tachdjian R, et al. *J Allergy Clin Immunol.* 2023;151(2 suppl):AB136. 6. Takhzyro [package insert]. Takeda Pharmaceuticals. 2023. 7. Haegarda [package insert]. CSL Behring. 2020. 8. Cinryze [package insert]. ViroPharma Biologics LLC, Takeda Pharmaceuticals. 2022.

ORLADEYO® ADMINISTERED VIA GRANULES

New dosage form

Pediatric Granules
(~ 2 x 3 mm)

Dosage instructions

Sprinkle granules on tongue
and swallow with water or milk

OR

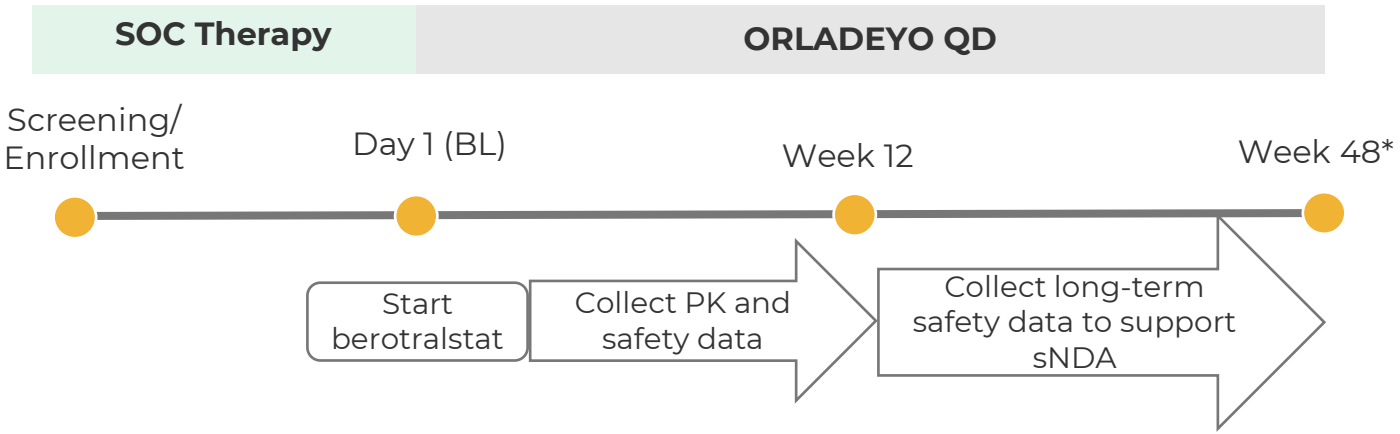
Sprinkle granules over 1 tablespoon of soft non-acidic food and consume immediately

- Chocolate pudding, baby food (peas, banana, carrot), mashed potatoes or sweet creamed corn

APEX-P: ORLADEYO® FOR THE TREATMENT OF HAE IN CHILDREN 2 TO < 12 YEARS OLD

Open-label trial across North America, Israel, UK and Europe (~15 sites) designed to evaluate the pharmacokinetics (PK) and safety of ORLADEYO in pediatric patients with HAE (ages 2 to < 12 years old)

- Goal is to determine the dosage that matches the exposure in adults
- 4 cohorts (N = 30) grouped by patient body weight



Submit US sNDA

2025

*Patients may continue to receive Orladeyo on study beyond 48 weeks. BL, baseline; HAE, hereditary angioedema; QD, once daily; PK, pharmacokinetics; sNDA, supplemental new drug application; SOC, standard of care; UK, United Kingdom; US, United States.

KEY TAKEAWAYS: ORLADEYO FOR PEDIATRICS

- Critical unmet need for oral treatment for children with HAE
- ORLADEYO can be administered via granules, making it easier to dose for children
- APEX-P is a pivotal, ongoing trial for ORLADEYO treatment in children with HAE
- On track to submit US sNDA in 2025

HAE, hereditary angioedema; sNDA, supplemental new drug application; US, United States.

PIPELINE PROGRAMS PAVE WAY FOR POTENTIAL THERAPEUTIC AREA GROWTH

Therapeutic area	Potential initial indications	Potential portfolio expansion
Allergy / Immunology	ORLADEYO® for HAE	• ORLADEYO pediatric
Dermatology	BCX17725 for NS	• Oral C5i + C2i combo for hidradenitis suppurativa (HS) • Bifunctional for bullous pemphigoid (BP)
Nephrology	BCX10013 for IgAN or C3G	• Bifunctional for lupus nephritis (LN) • BCX10013 + C2i oral combo for IgAN
Neurology	Oral C5i for gMG	• Oral C5i for neuromyelitis optica (NMO) • Oral C2i for multifocal motor neuropathy (MMN)
Hematology	Oral C2i for CAD	• Oral C2i for wAIHA
Ophthalmology	Avoralstat for DME	• Complement inhibitor for AMD and GA

Non-complement inhibitor programs

AMD, age-related macular degeneration; C2i, complement 2 inhibitor; C5i, complement 5 inhibitor; C3G, C3 glomerulopathy; CAD, cold agglutinin disease; DME, diabetic macular edema; GA, geographic atrophy; HAE, hereditary angioedema; IgAN, Immunoglobulin A nephropathy; gMG, generalized myasthenia gravis; NS, netherton syndrome; wAIHA, warm autoimmune hemolytic anemia.

DISCIPLINED CAPITAL ALLOCATION APPROACH

Anthony Doyle, Chief Financial Officer

DISCIPLINED CAPITAL ALLOCATION

- Strategic discovery process
- Disciplined approach to stage-gate investment
- Financial strength and future optionality

THANK YOU