J.P. MORGAN HEALTHCARE CONFERENCE

JON STONEHOUSE
PRESIDENT AND CHIEF EXECUTIVE OFFICER

JANUARY 2024

FORWARD-LOOKING STATEMENTS

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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

UNIQUELY POSITIONED TO CREATE SUSTAINABLE VALUE

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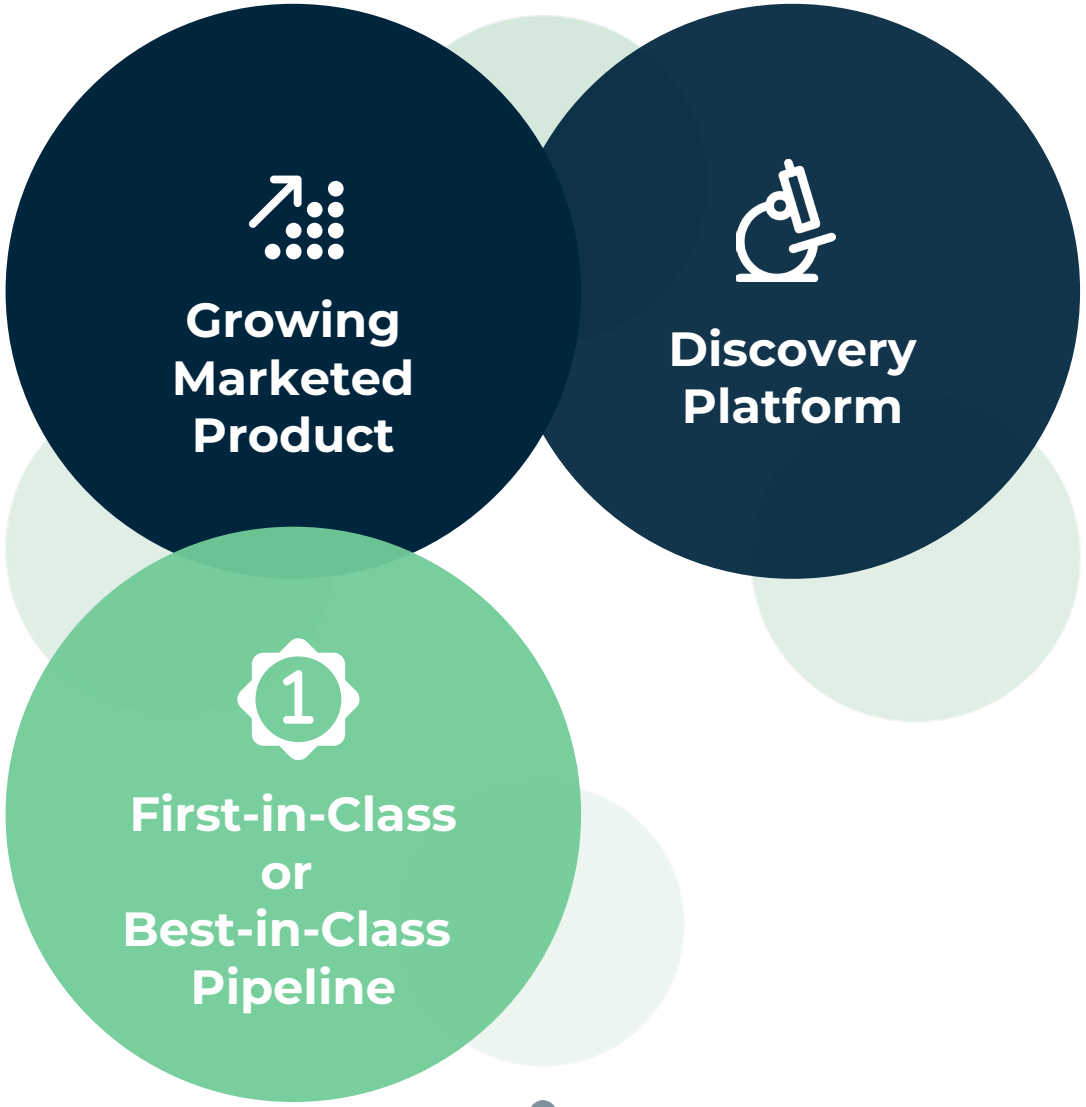
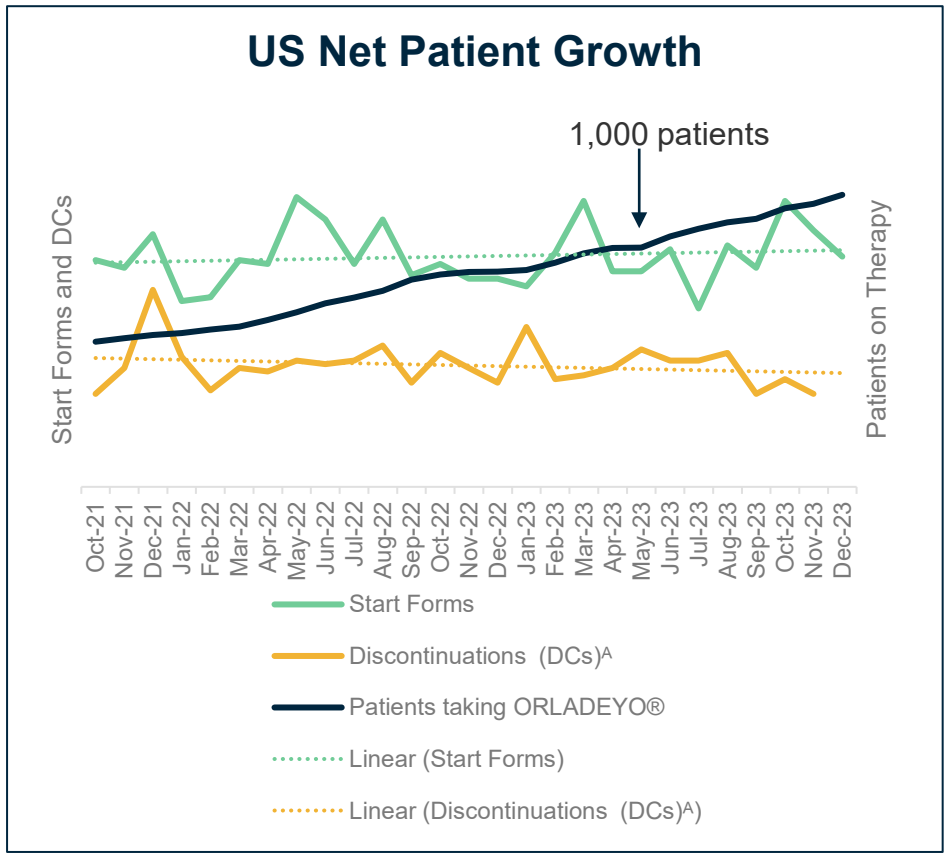


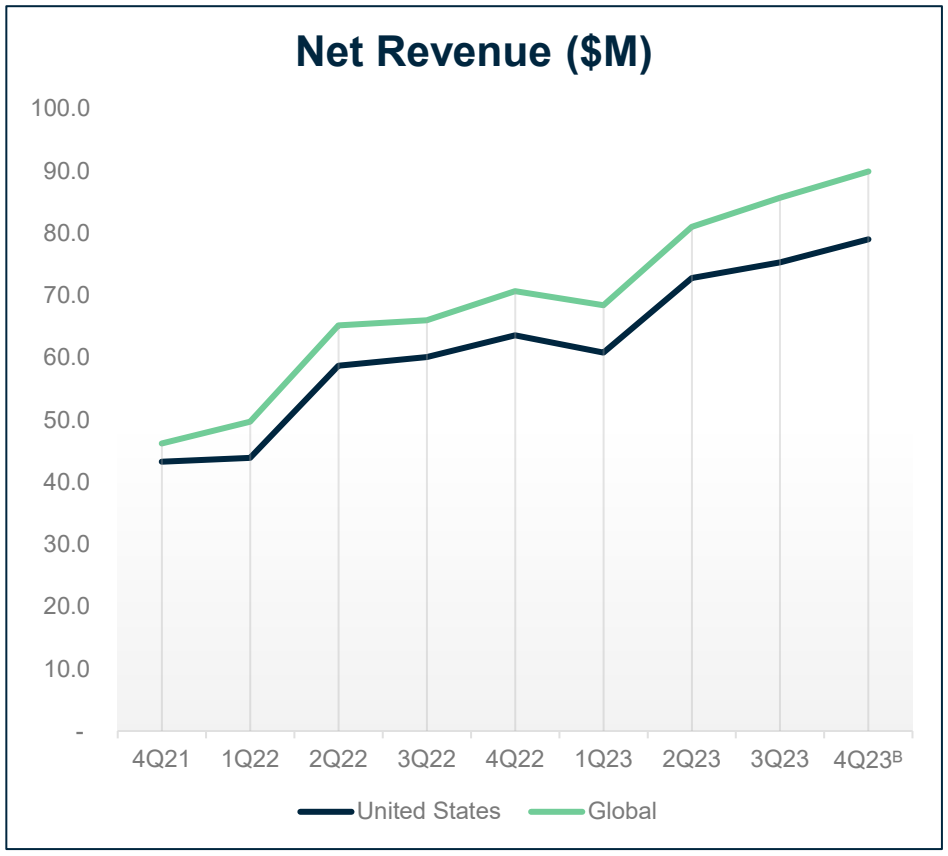
UNIQUELY POSITIONED TO CREATE SUSTAINABLE VALUE

orladeyo®

(berotralstat) capsules 150 mg

REVENUE $325M IN 2023 (THIRD YEAR) AND GROWING



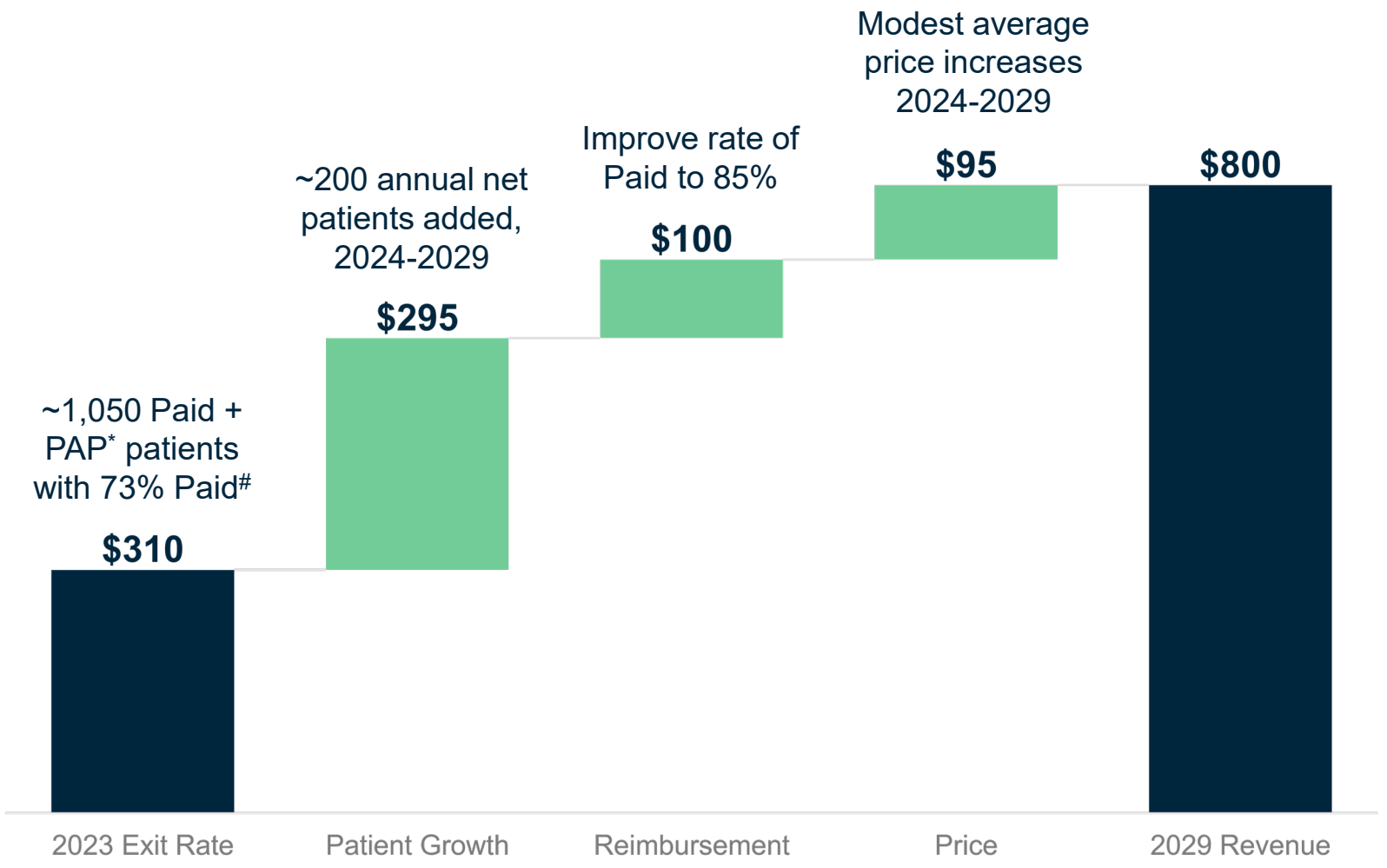


A – Discontinuations are dated to 30 days after the last shipment of ORLADEYO® to a patient.

B – 4Q23 revenue figures are preliminary and unaudited.

PATH TO $1B AT PEAK

$800M in the US by the end of the decade



Assumptions

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

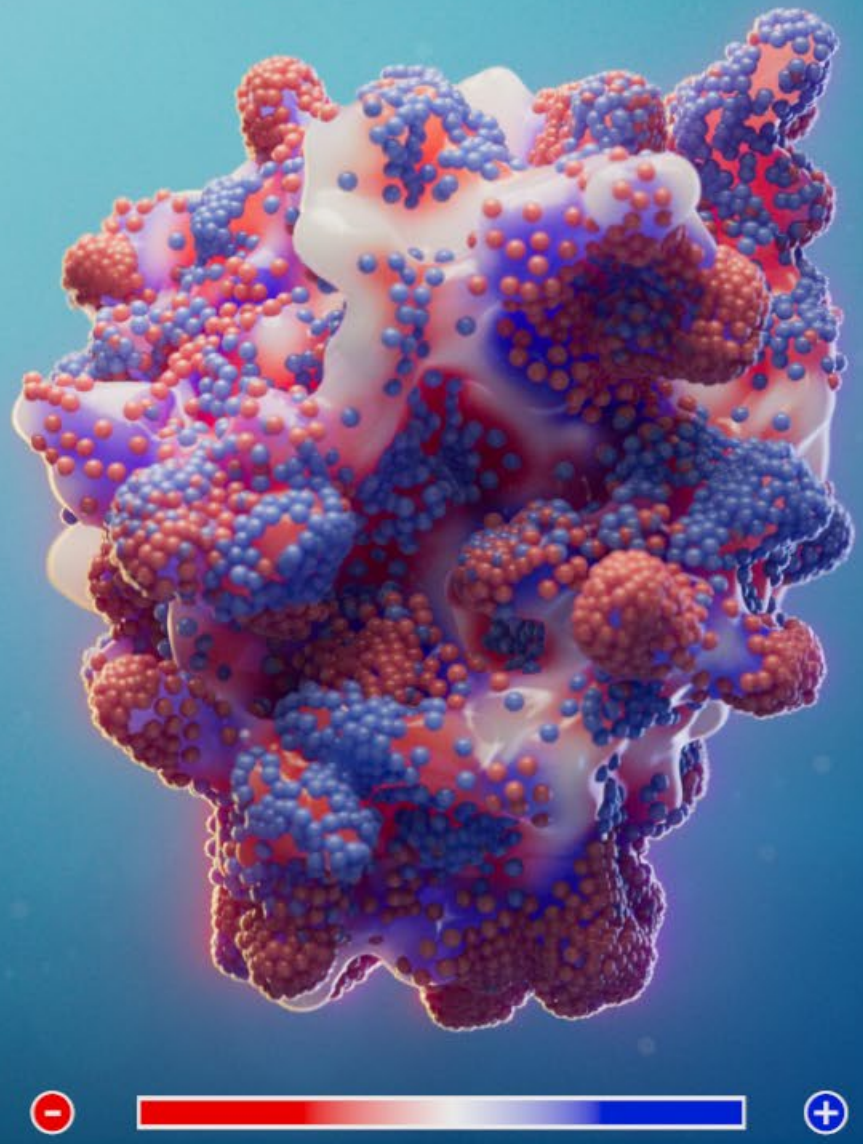
* PAP is the company's long-term patient assistance program

2023 year-end figures are approximate and represent a forward-looking base of revenue

$ in millions

Visibility to the atomic level

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



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.

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

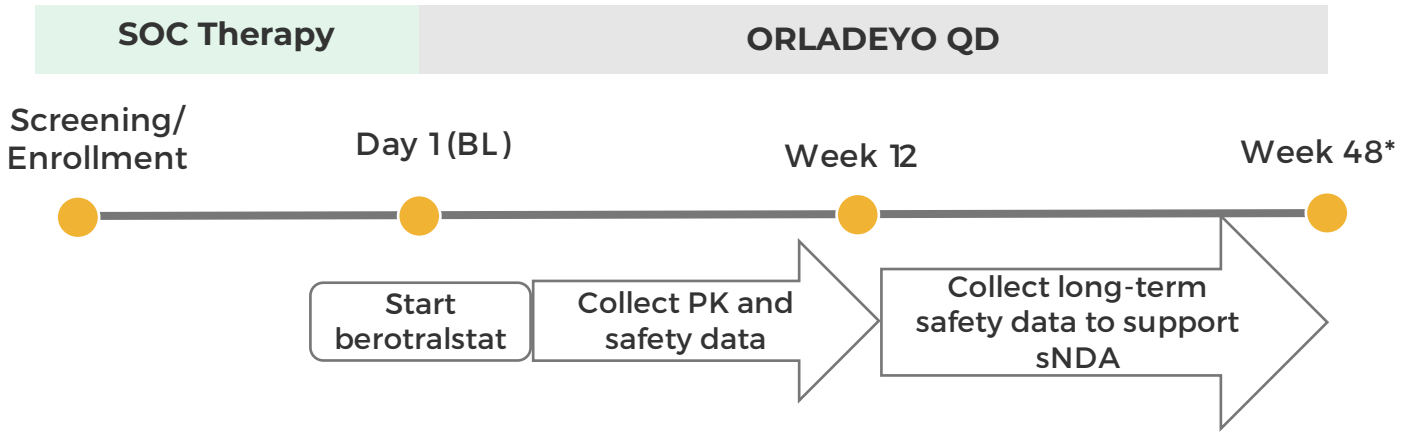
Sprinkle granules over 1 tablespoon of soft non-acidic food and consume immediately

- 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

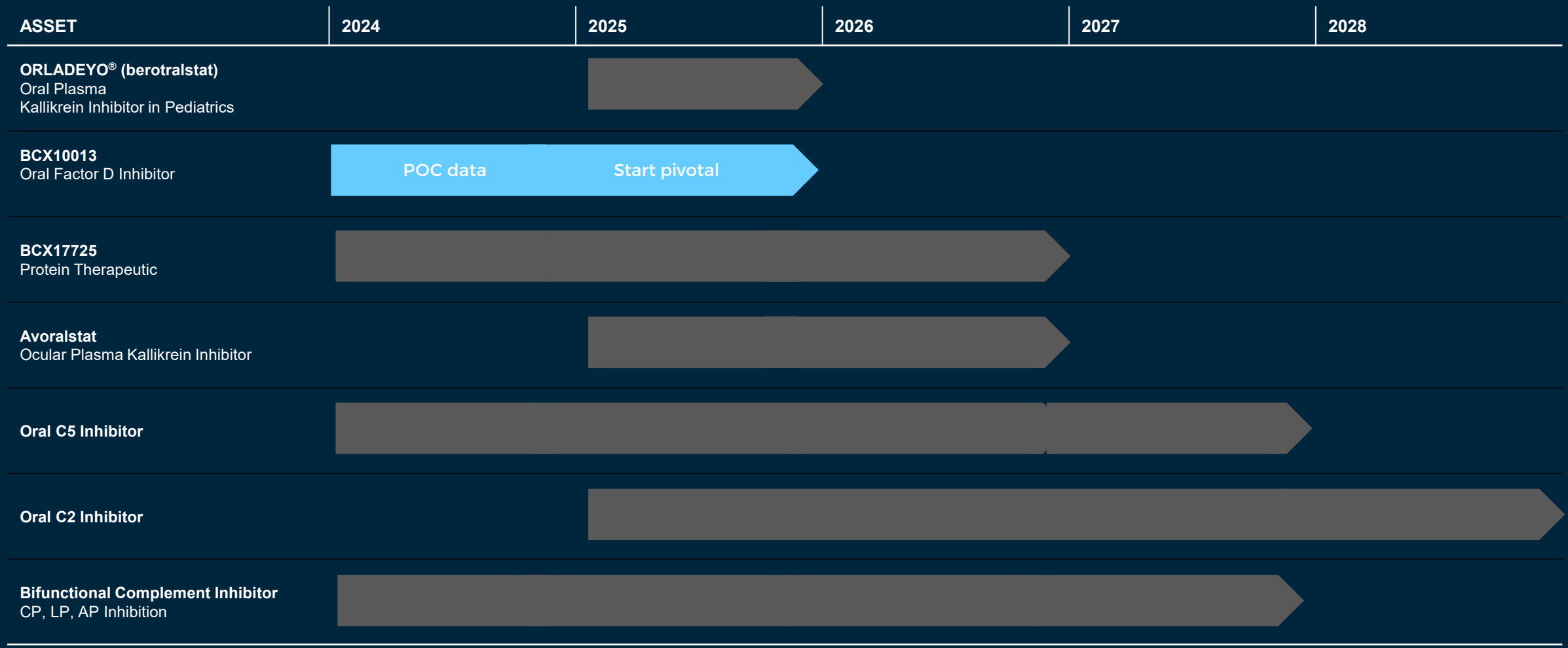


Submit US sNDA

2025

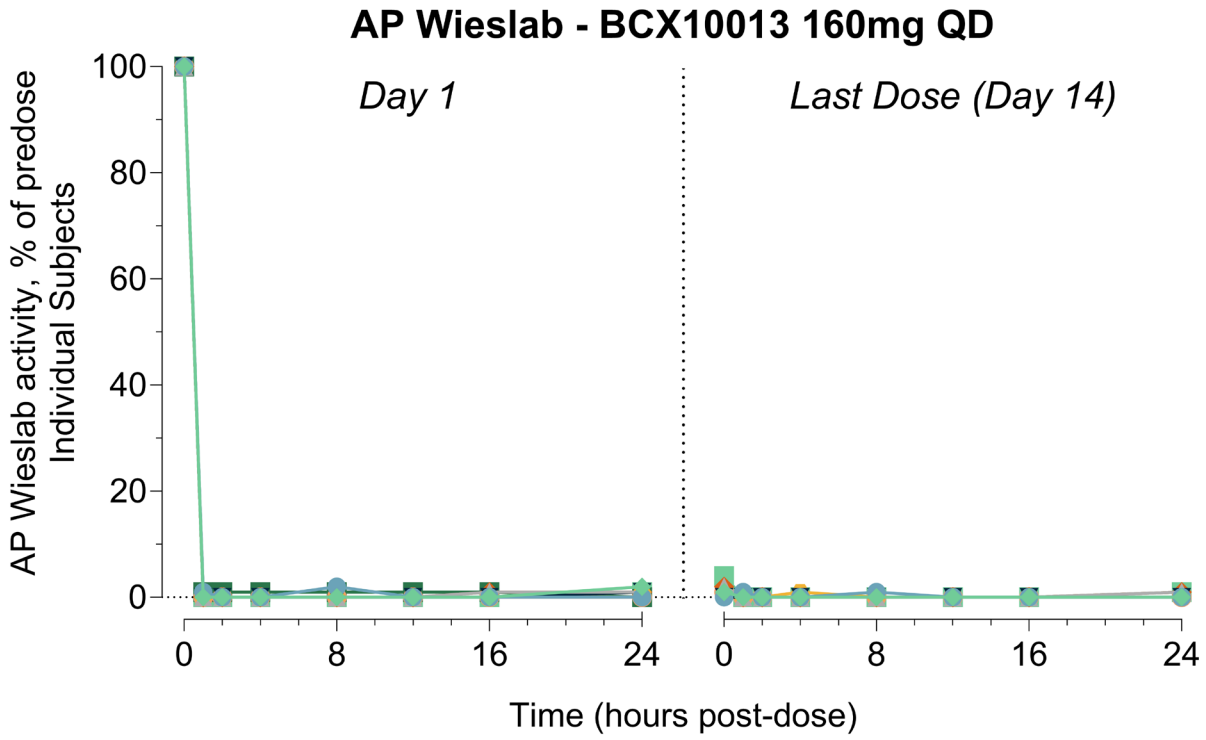
*Patients may continue to receive Orladeyo on study beyond 48 weeks. BL, baseline; HAE, hereditary angioedema; QD, once daily; PK, pharmacokinetics; sNDA, supplemental new drug application; SOC, standard of care; UK, United Kingdom; US, United States.

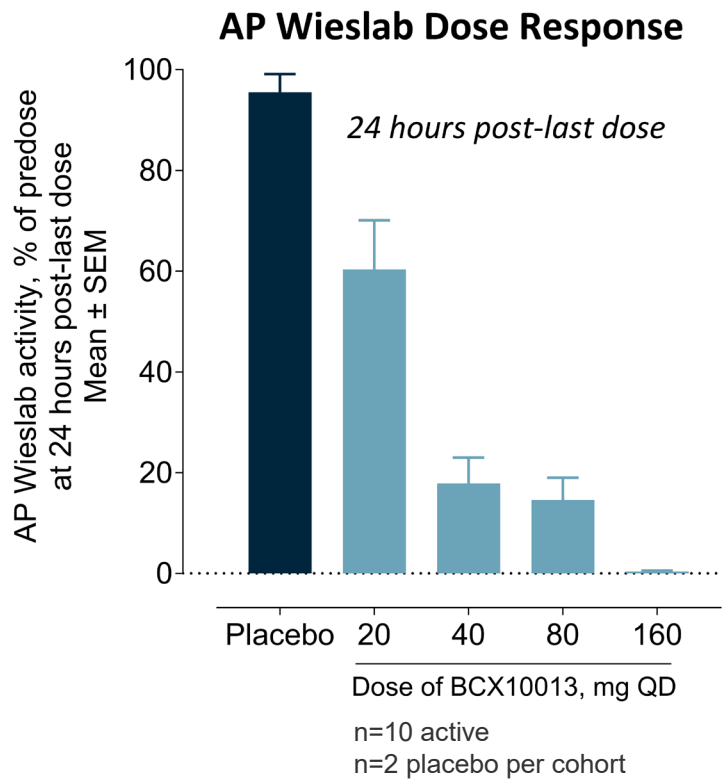
PIPELINE PROGRAM MILESTONES



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.

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.

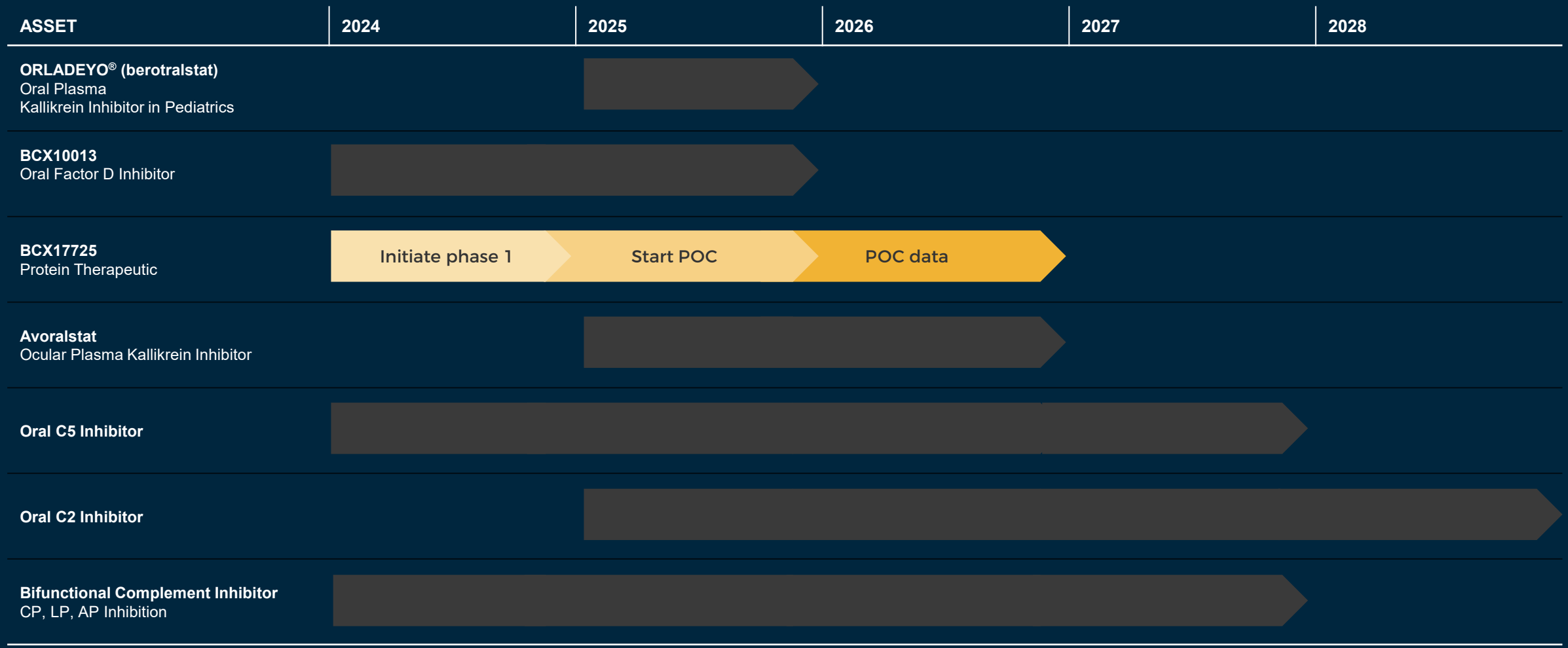
*On day 14, approximately 96% suppression pre-dose and 99% suppression 24 hours post-dose.
AP, alternative pathway; MAD, multiple ascending dose; MG, milligram; QD, once daily. BioCryst Pharmaceuticals data on file 2023.

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

Once-Daily 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.
Will partner Program to Accelerate Development	Allows BioCryst to **retain value**, **limit risk** and **focus resources** on other pipeline assets.

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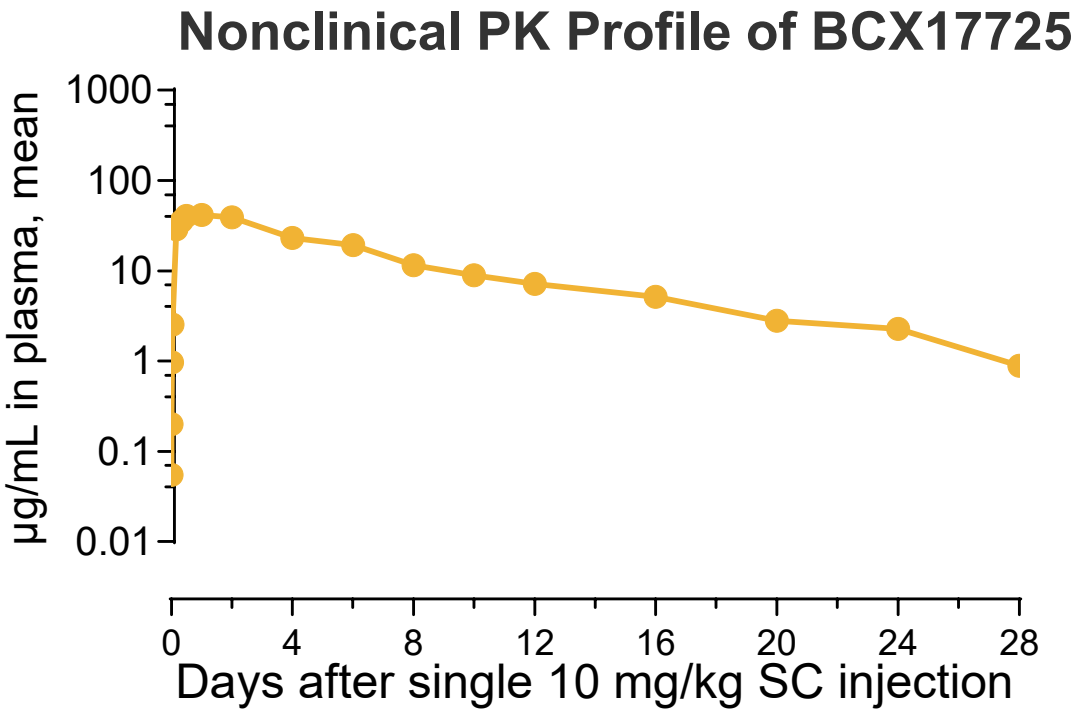
BCX17725 NONCLINICAL CHARACTERIZATION: POTENTIAL FOR BEST-IN-CLASS TARGETED TREATMENT FOR NETHERTON SYNDROME

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**

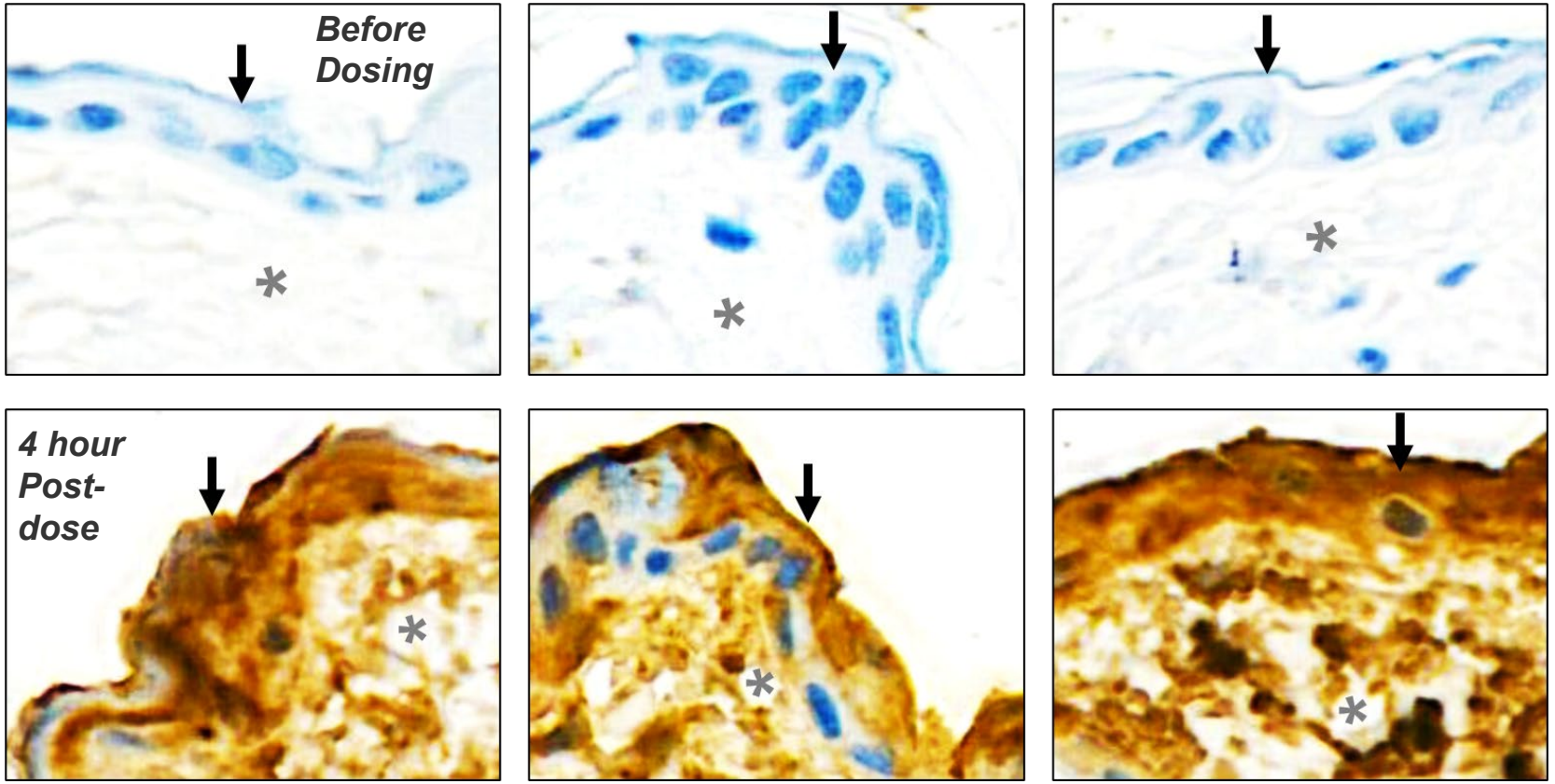
Low in-silico immunogenicity score – lower than unmodified normal human IgG-Fc, predicting **minimal risk of anti-drug antibodies**

1 million times more potent than natural ligand and 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**

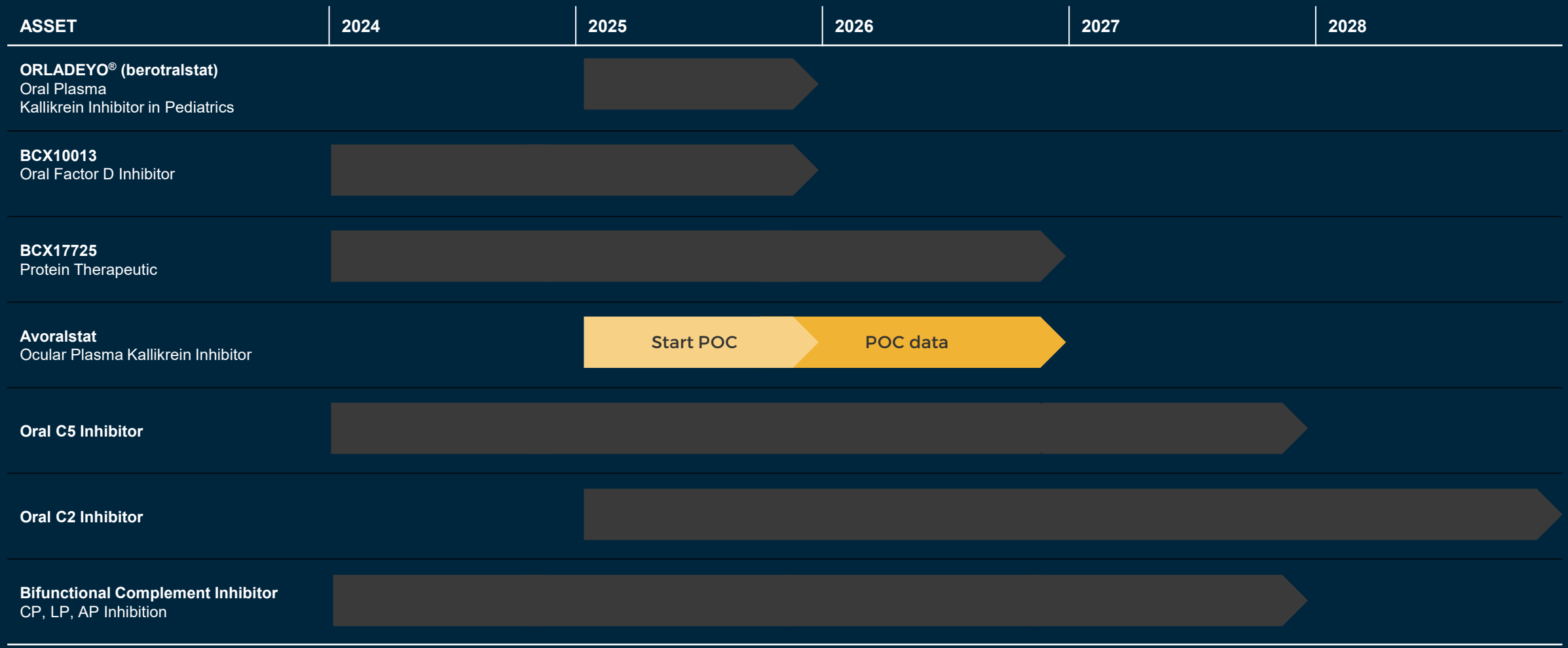
BCX17725 gets to the epidermis, the target tissue required for treating Netherton syndrome

↓ **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.

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

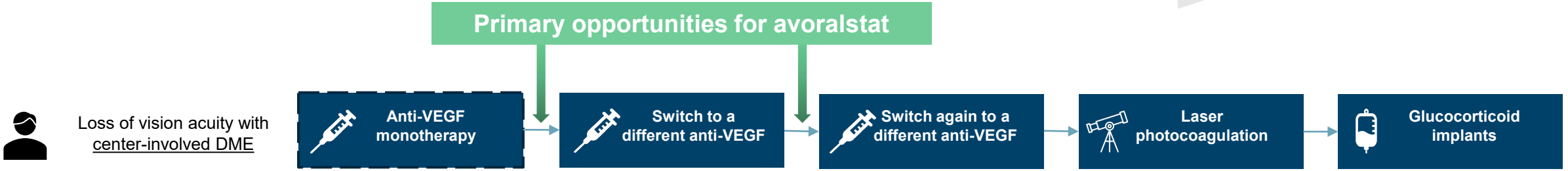
- Anti-VEGF therapies are the backbone of DME treatment and require intravitreal injections every 1 to 4 months[1,2]
- Current guidelines recommend up to 3 attempts at anti-VEGF therapy, with off-label Avastin (bevacizumab), Eylea (aflibercept), and Lucentis (ranibizumab) being the top 3 recommended 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.

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

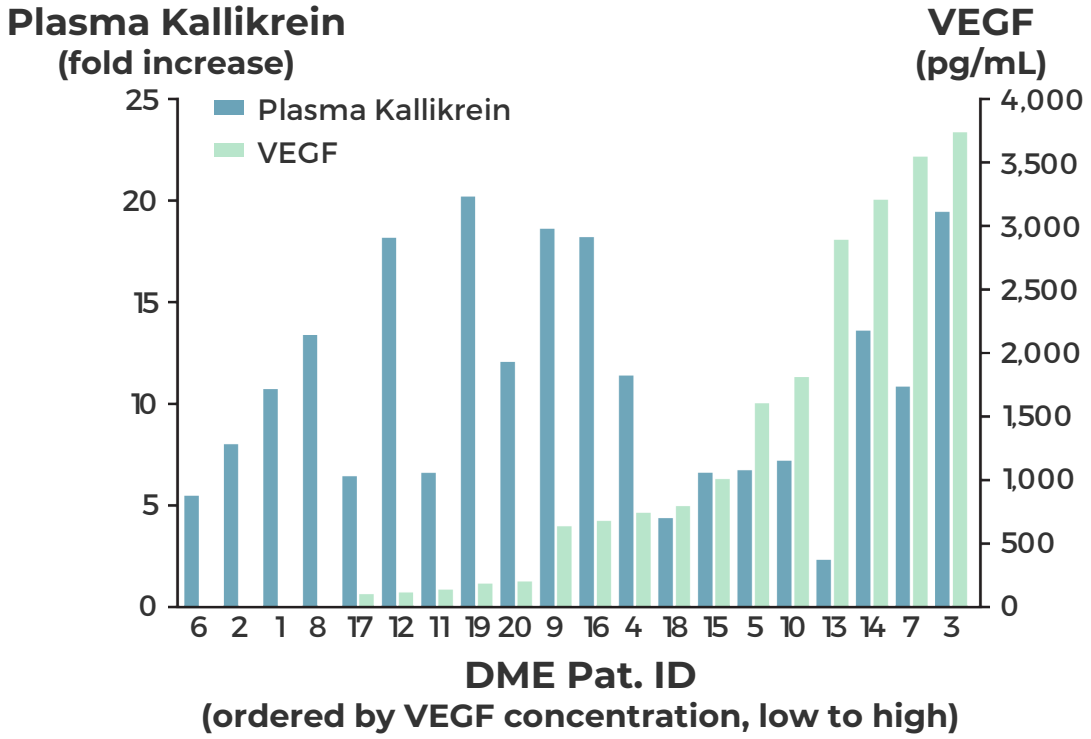
DME **continues to be most common cause of vision loss** in individuals with diabetes[1]

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

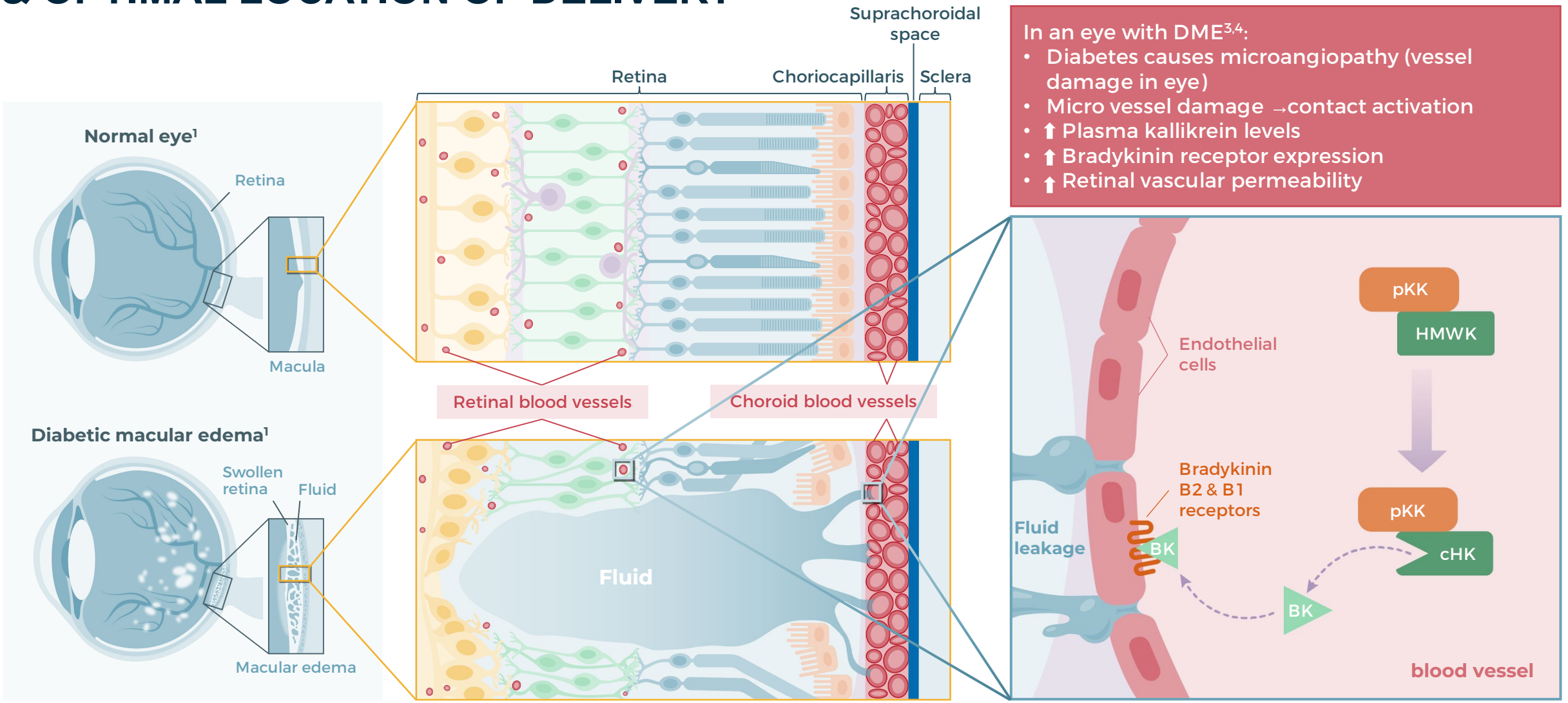


Immunoassays of DME vitreous samples[4]

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



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

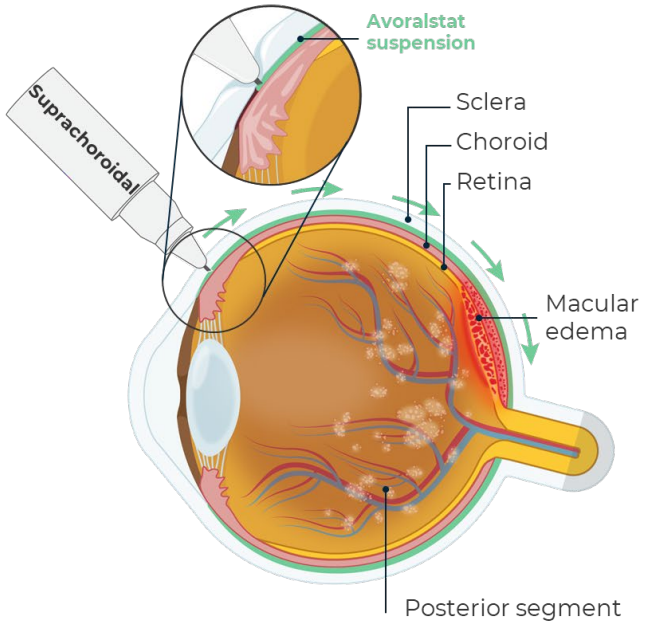
1. Trinh HM, et al. *World J Pharmacol.* 2016;5(1):1-14. 2. Yang S, et al. *Front. Pharmacol.* 2021;12:727870. 3. Kita T, et al. *Diabetes.* 2015;64(10):3588-3599. 4. Lang GE, et al. *TVST.* 2020;9(4)1-12. v.

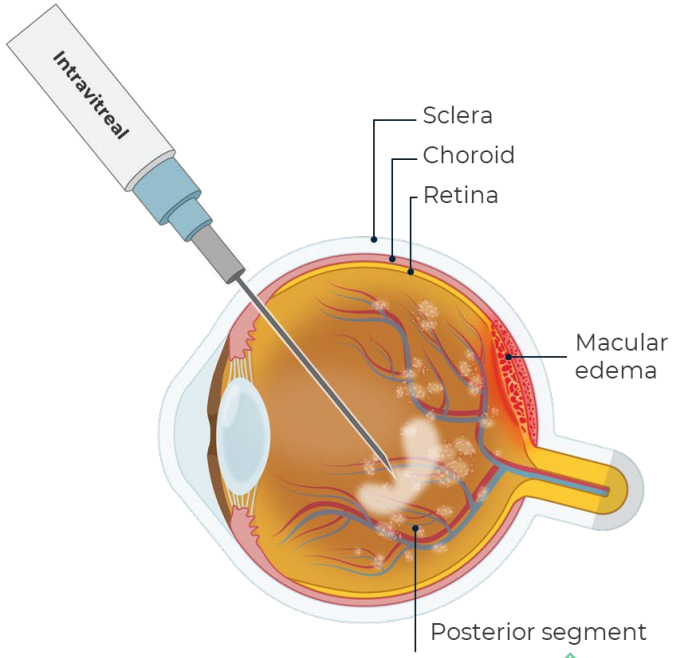
SUPRACHOROIDAL ADMINISTRATION OFFERS SEVERAL ADVANTAGES FOR DELIVERING AVORALSTAT TO TARGET TISSUES IN DME

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

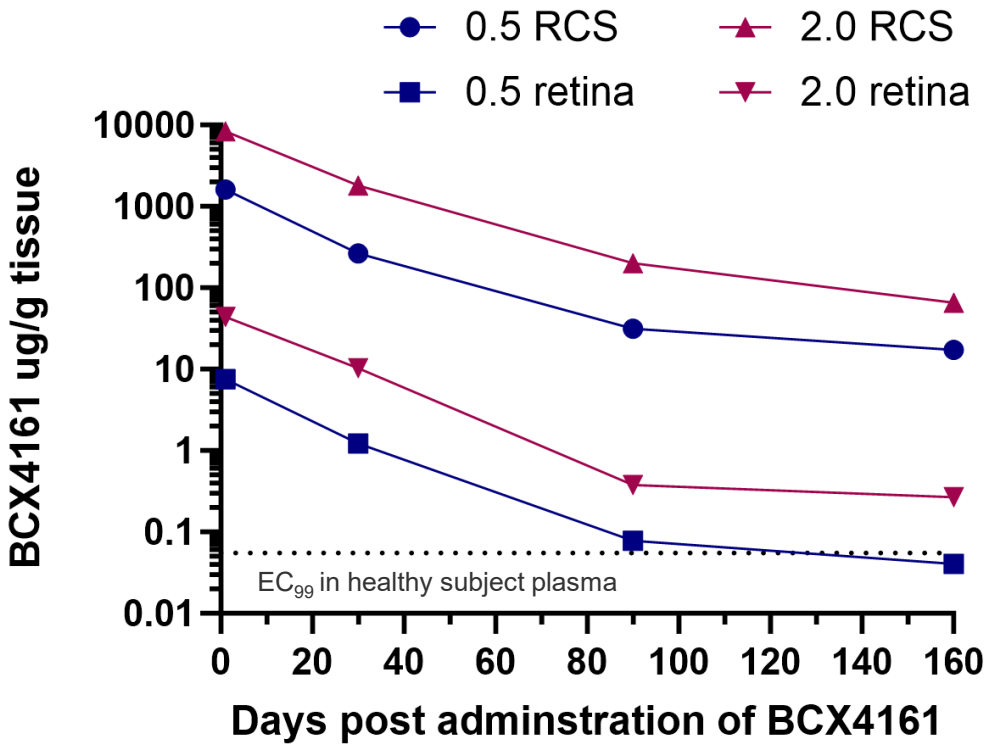
Suprachoroidal injector*





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

PRELIMINARY DATA SUPPORTS DURABLE EXPOSURE: DRUG RELEASE SUSTAINED THROUGH DAY 160 IN PRECLINICAL MODEL



	peripheral RPE-choroid-sclera (ng/g)	peripheral retina (ng/g)	Plasma (ng/mL)
0.5 mg/eye			
Day 1	1,610,000	7,548	21
Day 30	264,000	1,220	<1
Day 90	31,300	78	<1
Day 160	17,200	40	NA
2.0 mg/eye			
Day 1	8,387,500	44,030	56
Day 30	1,819,000	10,335	4
Day 90	201,500	380	<1
Day 160	65,500	267	NA

All points represent n = 4 eyes, except Day 160 which is 1 eye due to sample loss

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.

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

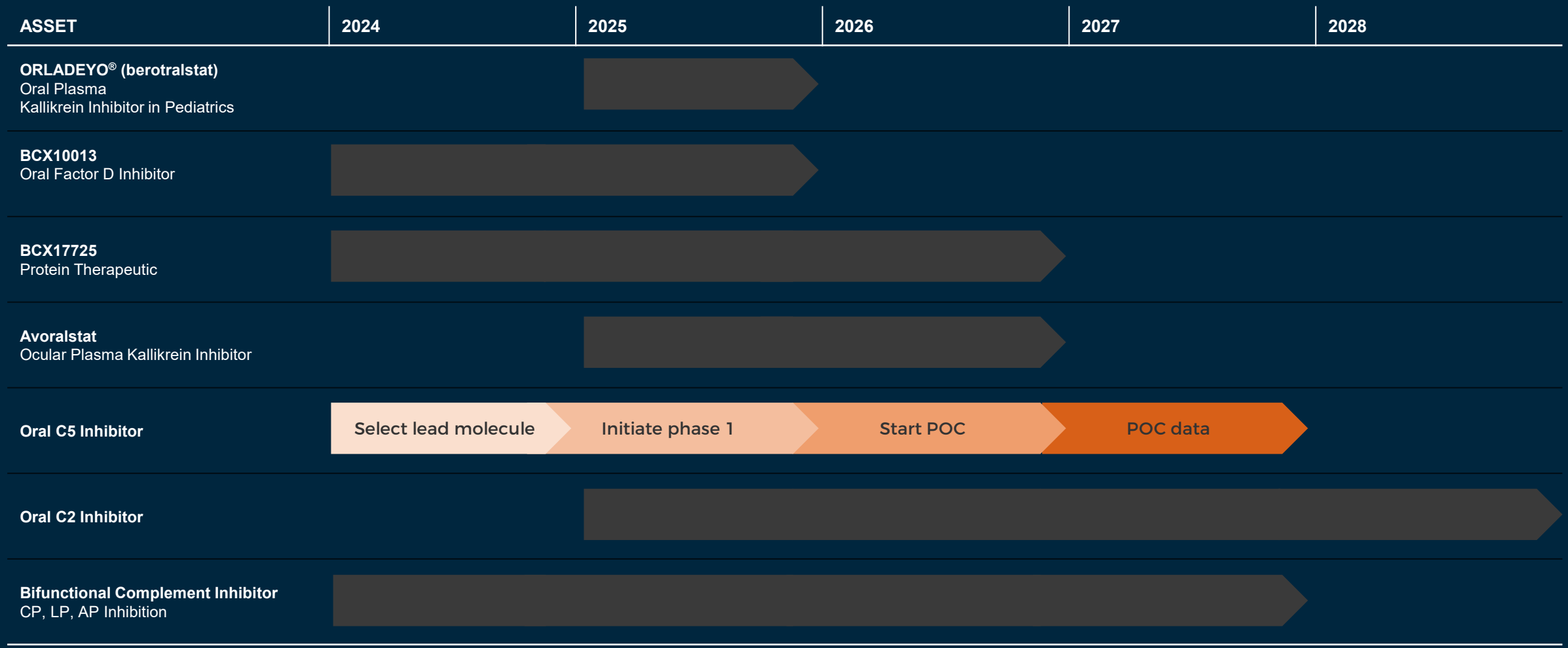
05 Diverse portfolio spreads development risk and increases commercial opportunity

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.

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.

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

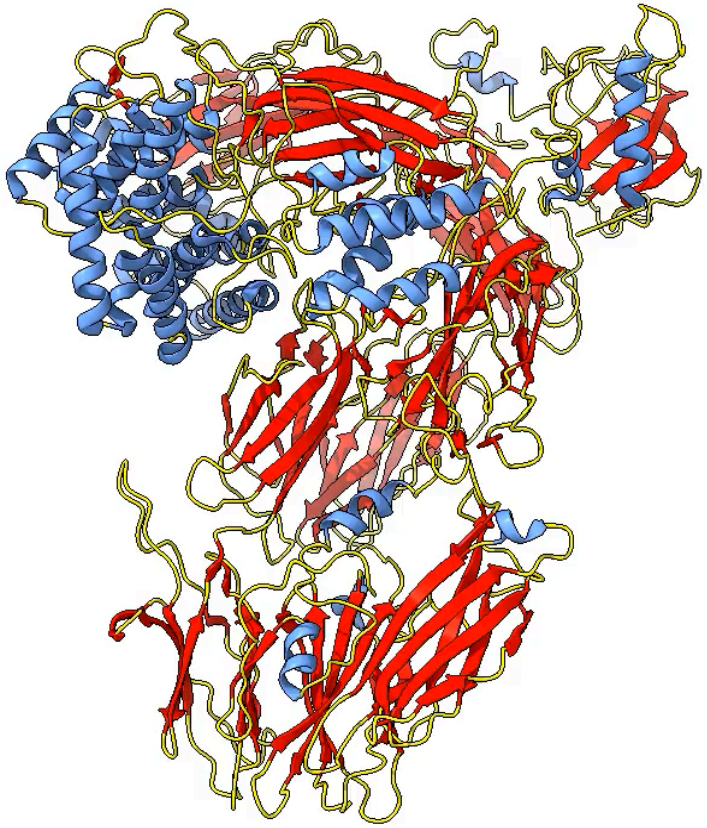
C5 is the initiator
of the terminal phase for **all 3 complement pathways.**[1]

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

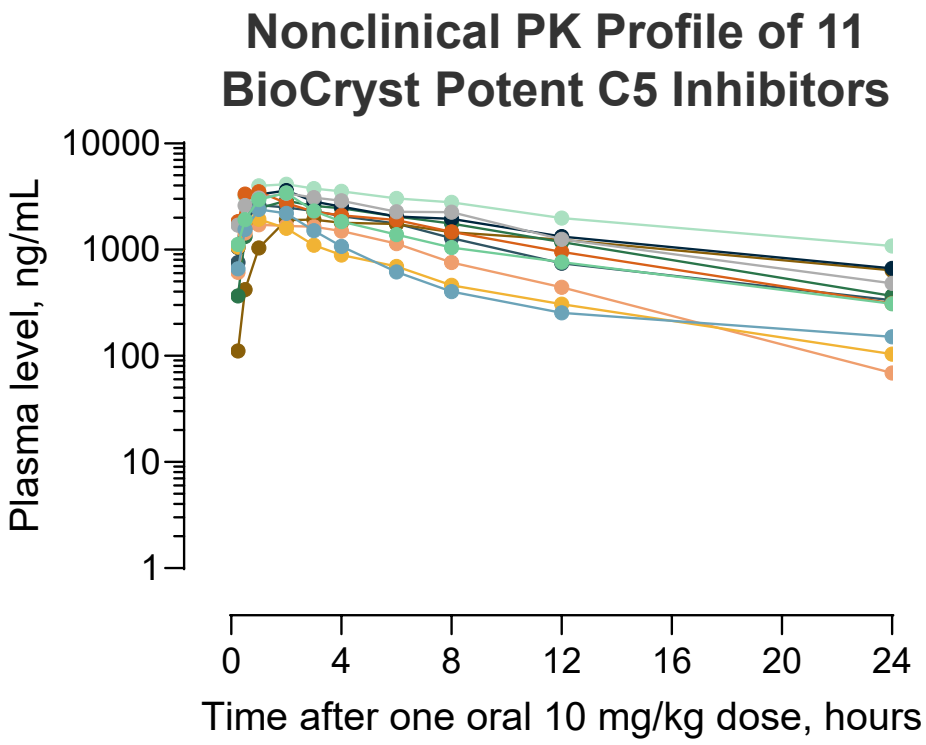


aHUS, atypical hemolytic uremic syndrome; ANCA-V, antineutrophilic cytoplasmic antibody associated vasculitis; C5, complement component 5; C5a, complement component 5a; gMG, generalized myasthenia gravis; NMOSD, neuromyelitis optica spectrum disorder; PNH, paroxysmal nocturnal hemoglobinuria. 1. Giorgio 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

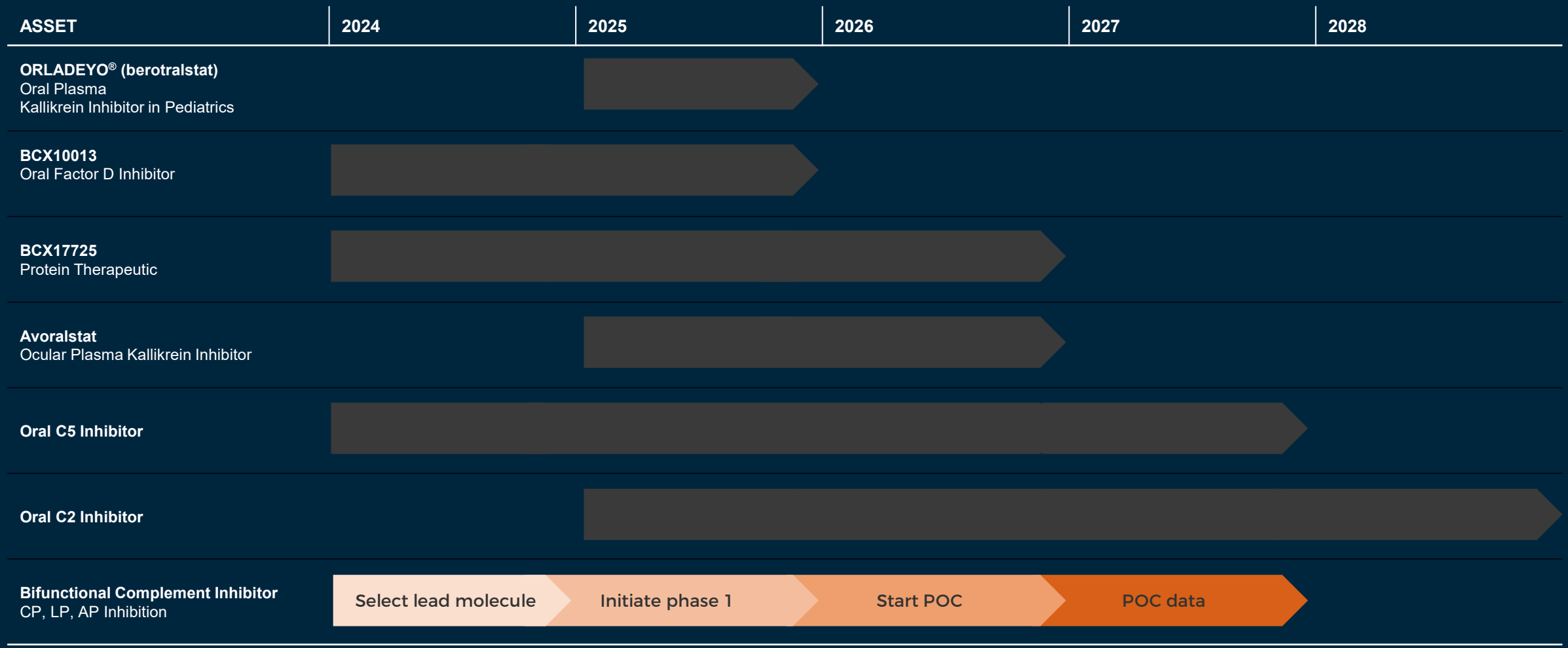
Goals are **high potency**, **selectivity**, **oral bioavailability**, **sustained exposure**, favorable metabolic profile, and typical small molecule physicochemical properties.

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.

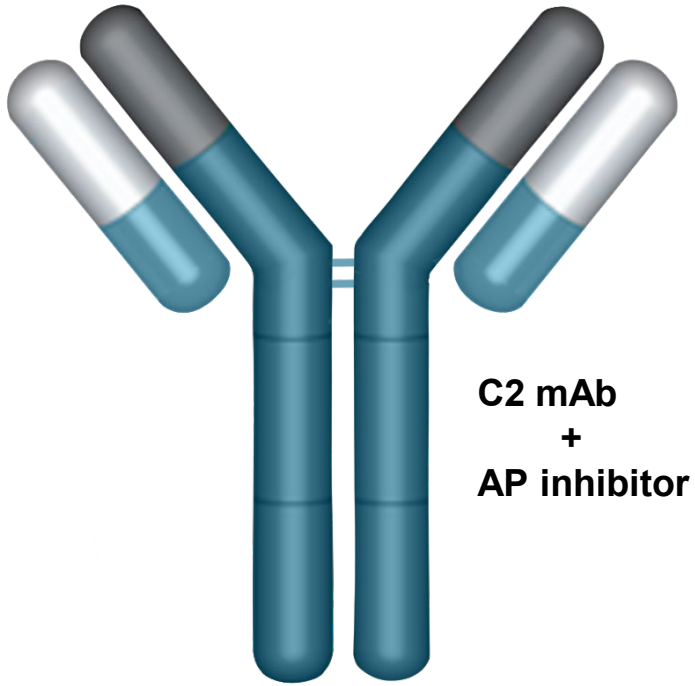
THE BIFUNCTIONAL INHIBITOR PROJECT COMBINES ANTI-C2 MAB WITH AP INHIBITOR IN ONE MOLECULE

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.

BIFUNCTIONAL COMPLEMENT INHIBITOR BLOCKS MULTIPLE COMPLEMENT PATHWAYS*

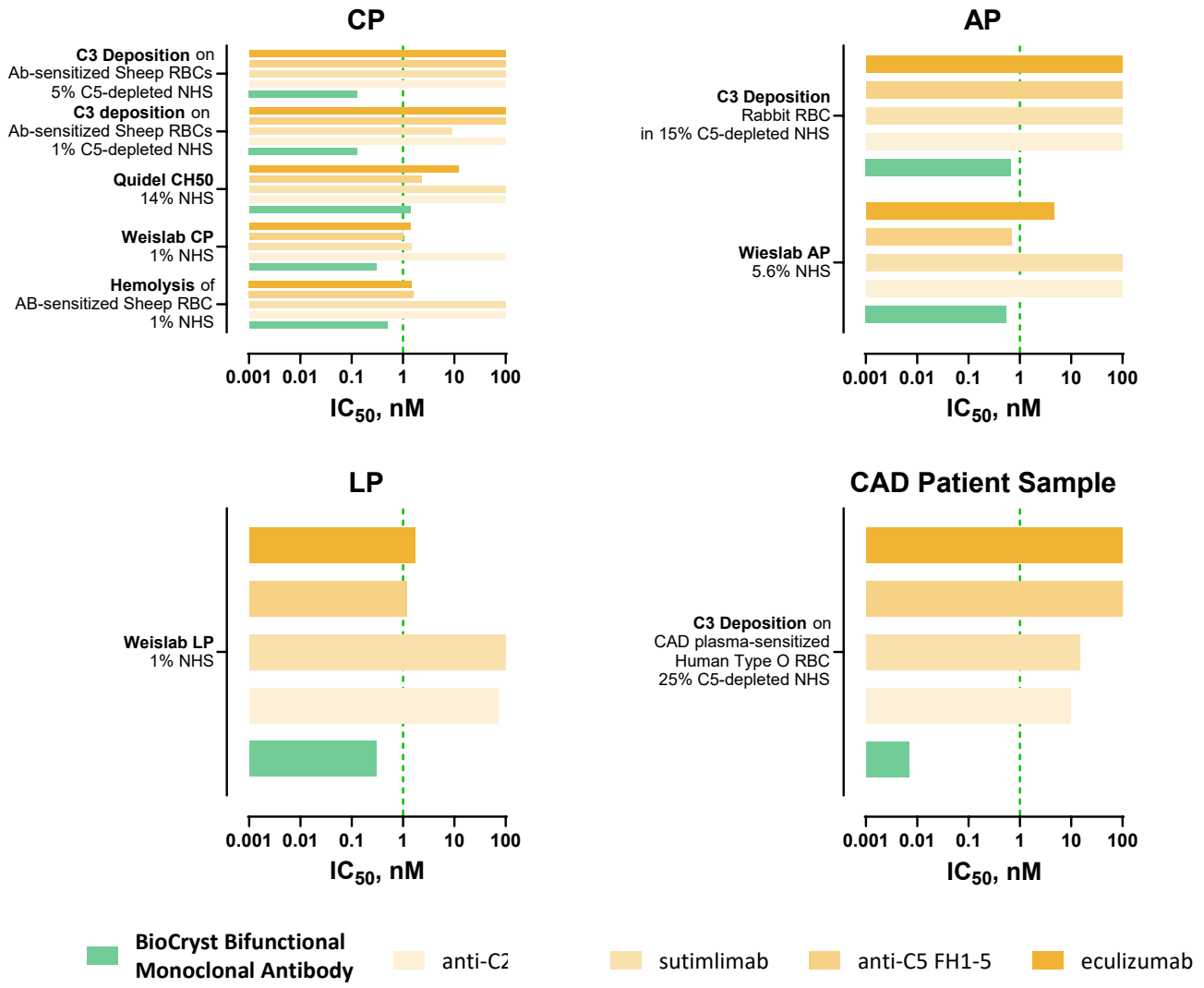
9 different assays evaluating CP, LP, AP, and combined CP+AP of complement

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.

GUIDANCE AND ACTIONS THIS YEAR

- FY 2024 ORLADEYO revenue between $380M to $400M
- FY 2024 operating expenses* less than revenue, at $365M-$375M
- FY 2024 R&D expenses reduced by $45M-$55M from prior guidance (Nov 2023 R&D Day)
  - With data from BCX10013 later in year will partner program or terminate program
  - Restructured R&D organization (59 jobs, 10% of total company headcount)
  - Postponed plans to expand Birmingham Discovery Center

*Not including non-cash stock compensation expense

CAPITAL MARKETS INDEPENDENCE

2024

Full year operating profit*

2025

Approaching quarterly positive EPS/cash flow in 2H

2026

Full year positive EPS/cash flow

Company does not intend to raise any additional funds, including not drawing the additional $150M in debt available from Pharmakon

*Not including non-cash stock compensation expense

UNIQUELY POSITIONED TO CREATE SUSTAINABLE VALUE