CENTESSA PHARMACEUTICALS

Corporate Overview

JANUARY 2022

Disclaimer

This presentation has been prepared by Centessa Pharmaceuticals plc (the “Company”) for informational purposes only and not for any other purpose. This presentation may contain forward-looking statements made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Statements in this presentation that are not statements of historical fact are forward-looking statements, including, without limitation, statements regarding ongoing and completed studies and their design and conduct; plans for continued development of our programs, including our global development plan and registrational path; our expectations with respect to the treatment paradigm for our programs, our asset-centric business model and the intended advantages and benefits thereof, research and clinical development plans, the scope, progress, results and costs of developing our product candidates or any other future product candidates, strategy, regulatory matters, including the timing and likelihood of success of obtaining approvals to initiate or continue clinical trials or market any products, market size and opportunity and our ability to complete certain milestones. Words such as "believe," "anticipate," "plan," "expect," "intend," "will," "may," "goal," "project," "estimate," "potential" and similar expressions are intended to identify forward loo king statements, though not all forward-looking statements necessarily contain these identifying words. These forward-looking statements are based on the beliefs of the Company's management as well as assumptions made by and information currently available to the Company. Such statements reflect the current views of the Company with respect to future events and are subject to known and unknown risks, including, without limitation, business, regulatory, economic and competitive risks, uncertainties, contingencies and assumptions about the Company, risks related to our ability to protect and maintain our intellectual property position; risks inherent in developing products and technologies; future results from our ongoing and planned clinical trials; our ability to obtain adequate financing to fund our planned clinical trials and other expenses; trends in the industry; the legal and regulatory framework for the industry; future expenditures risks related to our asset-centric corporate model; the risk that any one or more of our product candidates will not be successfully developed and commercialized; the risk that the results of preclinical studies or clinical studies will not be predictive of future results in connection with future studies; and risks related to the COVID-19 pandemic including the effects of the Delta variant and the other risk factors contained in our filings with the U.S. Securities and Exchange Commission. In light of these risks and uncertainties, the events or circumstances referred to in the forward-looking statements may not occur. The actual results may vary from the anticipated results and the variations may be material. These forward-looking statements should not be taken as forecasts or promises nor should they be taken as implying any indication, assurance or guarantee that the assumptions on which such forward looking statements have been made are correct or exhaustive or, in the case of the assumptions, fully stated in this presentation. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date this presentation is given.

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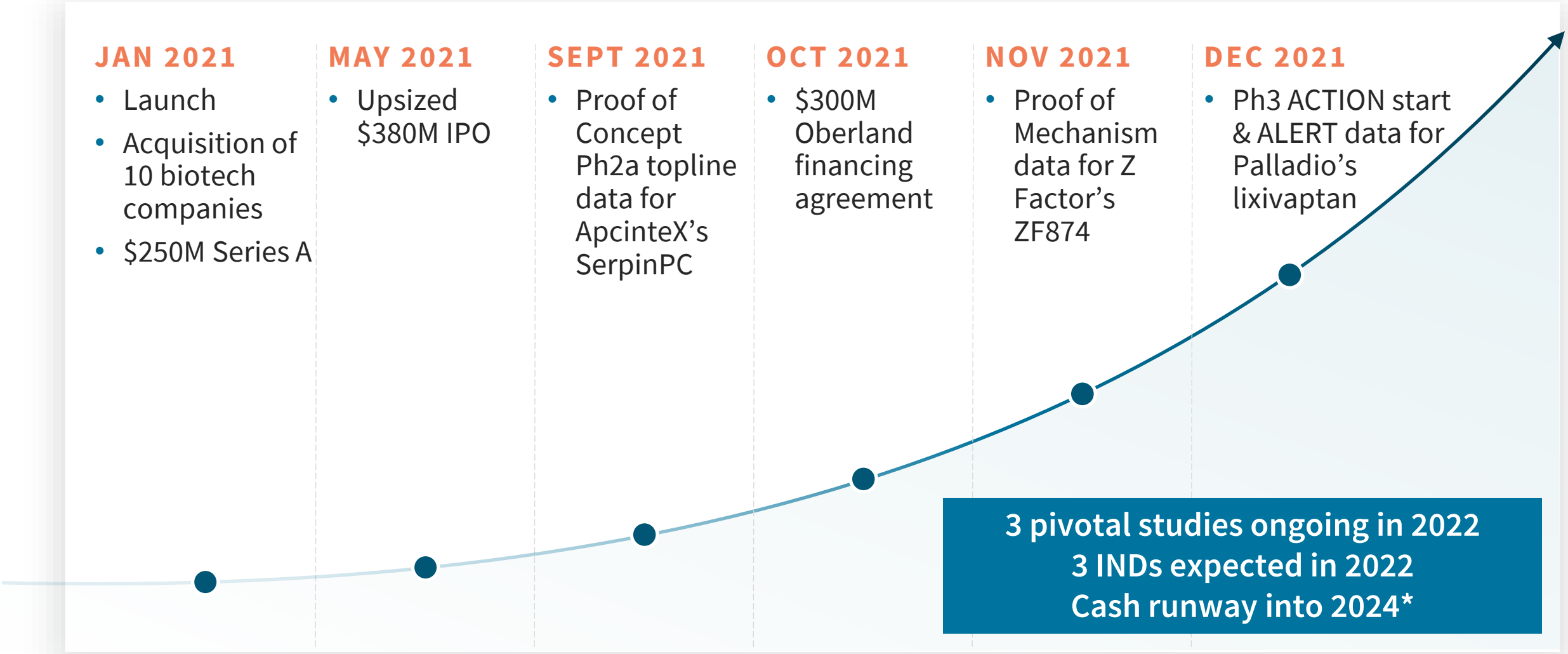
Mission

Deliver consequential medicines to patients by striving to make the unprecedented possible

Milestones

Significant momentum with 2021 accomplishments



* Company expects the cash and cash equivalents as of Sept 30, 2021, plus the net proceeds of the first tranche, supplemented by the additional funds available under the Oberland Facility, if drawn, to fund its operations into 2024.

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Combining a biotech's **agility** and **capital efficiency** with a pharma company's experienced **leadership team** and **diversified pipeline**

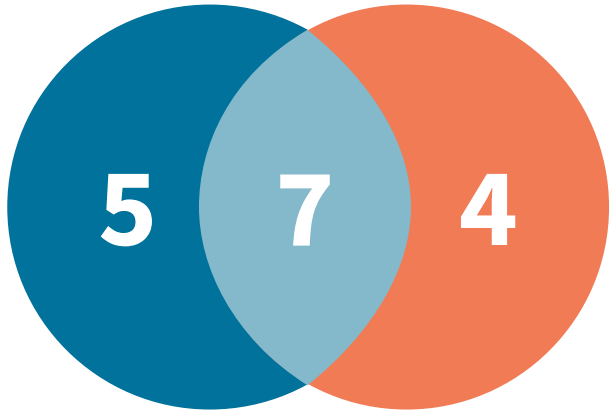
POTENTIAL

We start with strong biological rationale and aim to develop potential **first-in-class / best-in-class** assets, with programs that could each be **$1B+ opportunities**

16 Programs

12 Have Precedented Human Activity

11 Have Prior Learning with Human Genetics



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Centessa by the numbers

10 Wholly-owned Companies

- **300** Active Patents
- **1000+** Published Papers[1]
- **20+** Subject-matter Experts

16 Disclosed Programs

- **4** Assets in the Clinic
- **7** Oncology Assets
- **9** Rare Disease Assets[2]

1. Publications by members of the Centessa team
2. Excluding oncology assets

Management team with deep pharma & biotech drug development experience

SAURABH SAHA MD PhD
Chief Executive Officer

Bristol Myers Squibb · NOVARTIS · Delinia · ATLASVENTURE · McKinsey&Company

ANTOINE YVER MD MSc
Chief Medical Officer

Daiichi-Sankyo · AstraZeneca · CHUGAI · Johnson&Johnson · Aventis · Schering-Plough · MERCK · RHÔNE-POULENC · als

DAVID GRAINGER PhD
Chief Innovation Officer

medicxi · RxCelerate · totalscientific · Index Ventures

GREG WEINHOFF MD MBA
Chief Financial Officer

ARVELLE THERAPEUTICS · AXOVANT · Amicus Therapeutics · Morgan Stanley · CHL HEALTHCARE PARTNERS

DAVID CHAO PhD
Chief Administrative Officer

BIOMED VALLEY DISCOVERIES · STOWERS INSTITUTE FOR MEDICAL RESEARCH · NOVARTIS · nectagen · McKinsey&Company

TIA BUSH
Chief Quality Officer

AMGEN

MARELLA THORELL
Chief Accounting Officer

PALLADIO BIOSCIENCES · Campbell's · realm THERAPEUTICS · EY

THOMAS TEMPLEMAN PhD
Chief Technology Officer

Nuvation Bio · AXOVANT · Hospira · graybug · MEDIVATION · Johnson&Johnson · LIQUIDIA TECHNOLOGIES

IQBAL HUSSAIN
General Counsel

ReedSmith · Johnson&Johnson · ROPES&GRAY · SLAUGHTER AND MAY

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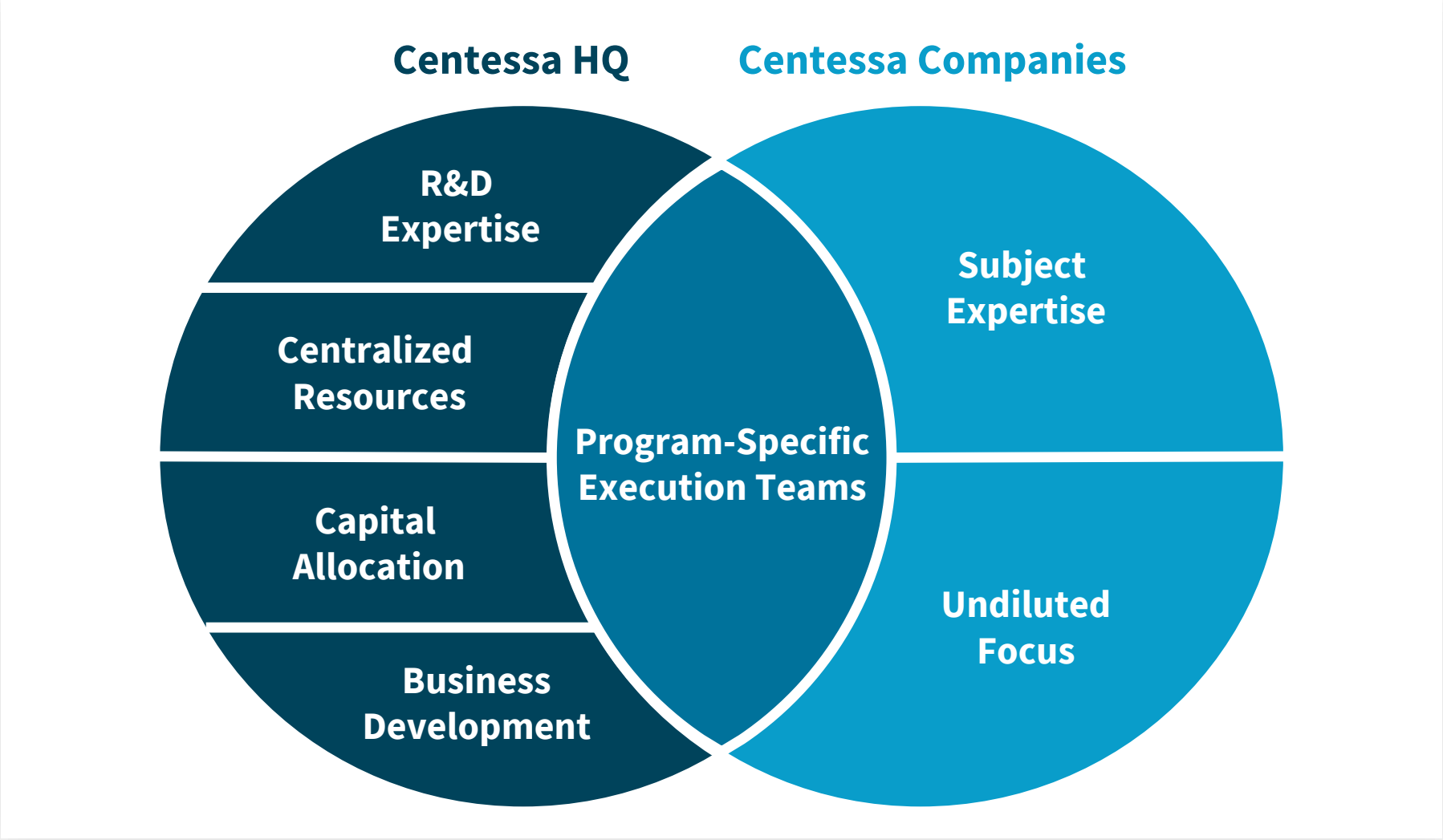
Agile, capital efficient, team-based model focused on value creation through innovation



Pipeline ~ Expecting Large Pharma-like IND Productivity in 2022-23

Company	Disease	Mechanism	Discovery	Lead Op / IND-enabling	Phase 1	Phase 2	Phase 3
Palladio Biosciences	Autosomal Dominant Polycystic Kidney Disease	Vasopressin V2 Receptor Antagonist	Lixivaptan				
ApcinteX	Hemophilia A and B	Activated Protein C Inhibitor	SerpinPC				
Pega-One	Cutaneous Squamous Cell Carcinoma	Anti-EGFR mAb	Imgatuzumab				
Z Factor	Alpha-1 Antitrypsin Deficiency	Z-A1AT Folding Corrector	ZF874				
			ZF887				
Morphogen-IX	Pulmonary Arterial Hypertension	BMP9 Engineered Variant	MGX292				
Capella BioScience	Idiopathic Pulmonary Fibrosis	Anti-LIGHT mAb	CBS001				
	Systemic Sclerosis and Lupus Erythematosus	Anti-BDCA2 mAb	CBS004				
LockBody Therapeutics	Solid Tumors	PD-L1-CD47 LockBody	LB1				
		PD-L1-CD3 LockBody	LB2				
Orexia Therapeutics	Narcolepsy Type 1	OX2R Agonist (Oral)					
		OX2R Agonist (Intranasal)					
Janpix	Acute Myeloid Leukemia	Dual-STAT3/5 Degrader					
PearlRiver Bio	Non-Small Cell Lung Cancer	EGFR-C797S Inhibitor					
		EGFR-Ex20 Inhibitor					
		EGFR-Next Gen					

Clinical-stage companies

By the end of 2023, all Centessa companies aim to have assets in the clinic

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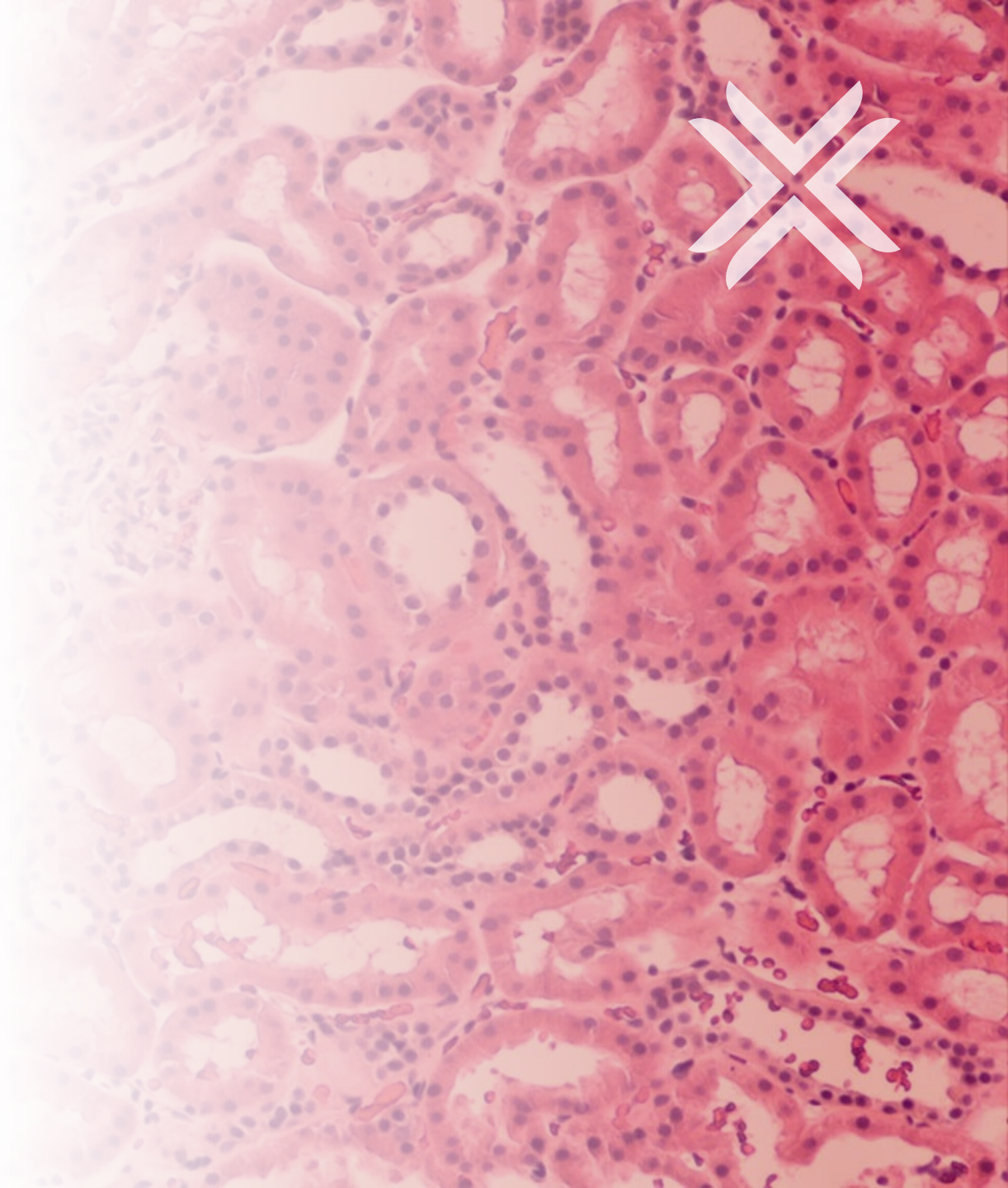
Palladio Biosciences

Lixivaptan



Differentiation

Potential benefits of lixivaptan

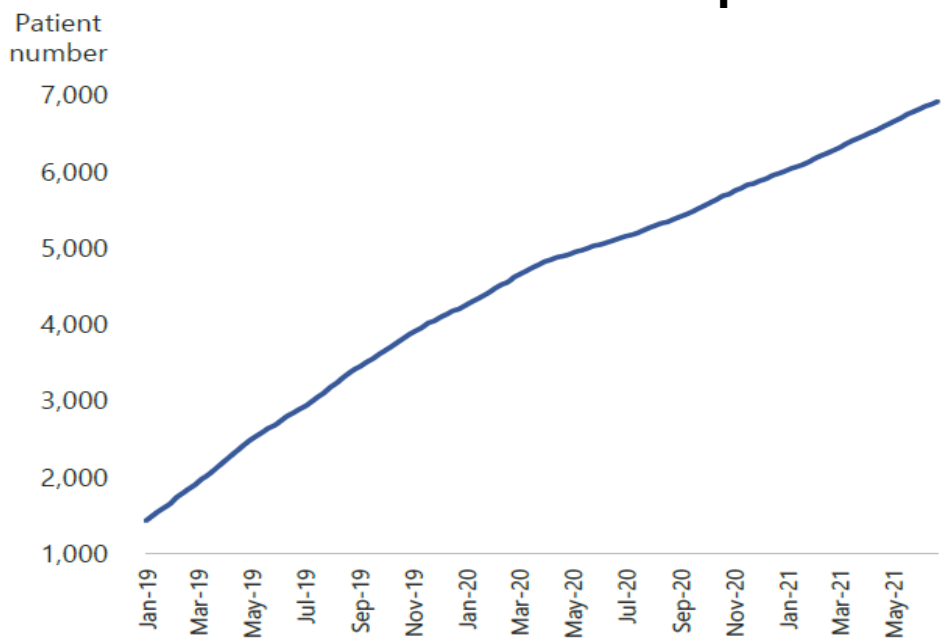
Potential to be a **best-in-class** treatment for ADPKD

Potential to **avoid liver toxicity** associated with the only approved treatment, tolvaptan

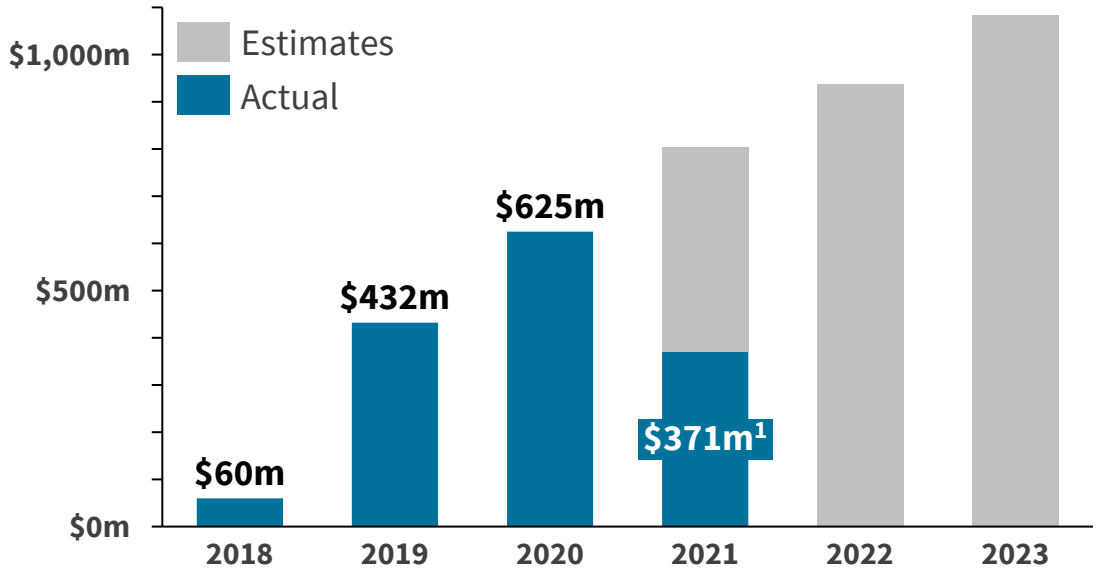
Potential for **comparable efficacy** to tolvaptan with a positive benefit/risk ratio

Rapid adoption of JYNARQUE® validates market opportunity

Cumulative number of new patient in US



US Sales of JYNARQUE® for ADPKD



JYNARQUE® approved April 2018 in the US with a black-box warning and restrictive REMS requiring frequent monitoring; on track to exceed $1B annual sales by 2023 despite COVID impacts

1. 1H 2021 sales

Source: Otsuka Holdings Q2 2021 Financial Results Presentation; Evaluate Pharma

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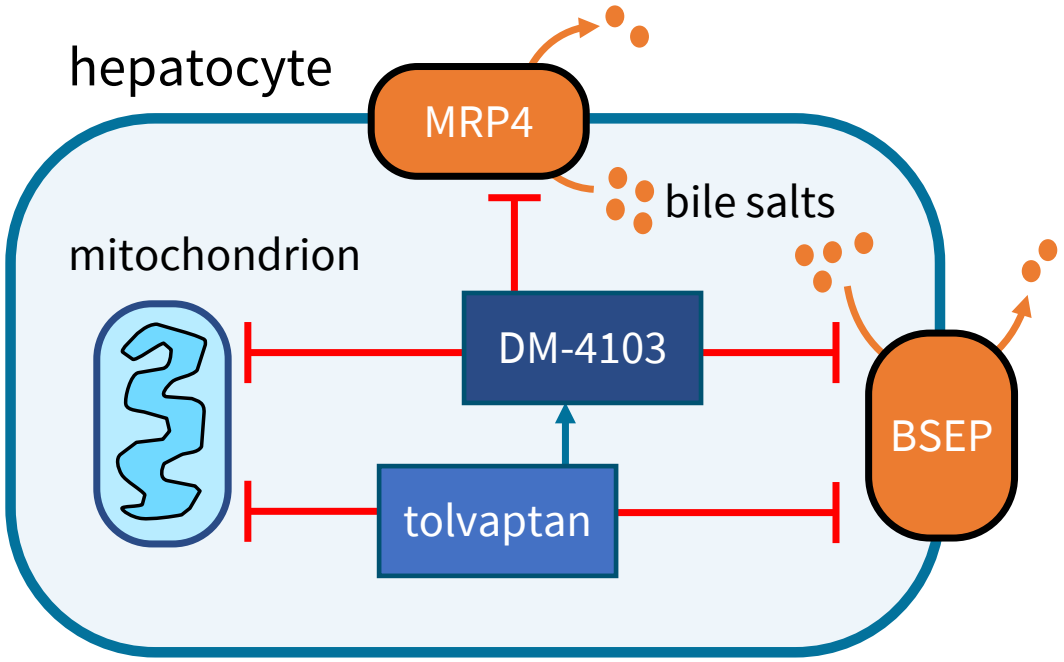
Need for a safe treatment for ADPKD, without drug-induced liver injury (DILI) risk



- Tolvaptan can cause liver toxicity via a **tolvaptan-specific metabolite**
- Liver toxicity believed to be an **off-target effect**
- **Lixivaptan has a different structure** and different metabolites than tolvaptan

Source: Adapted from Yang et al., Clin Pharm & Thera 2014; Slizgi et al., Tox Sci 2015; Woodhead et al., Tox Sci 2016; Mosedale and Watkins, Clin Pharm & Thera 2017

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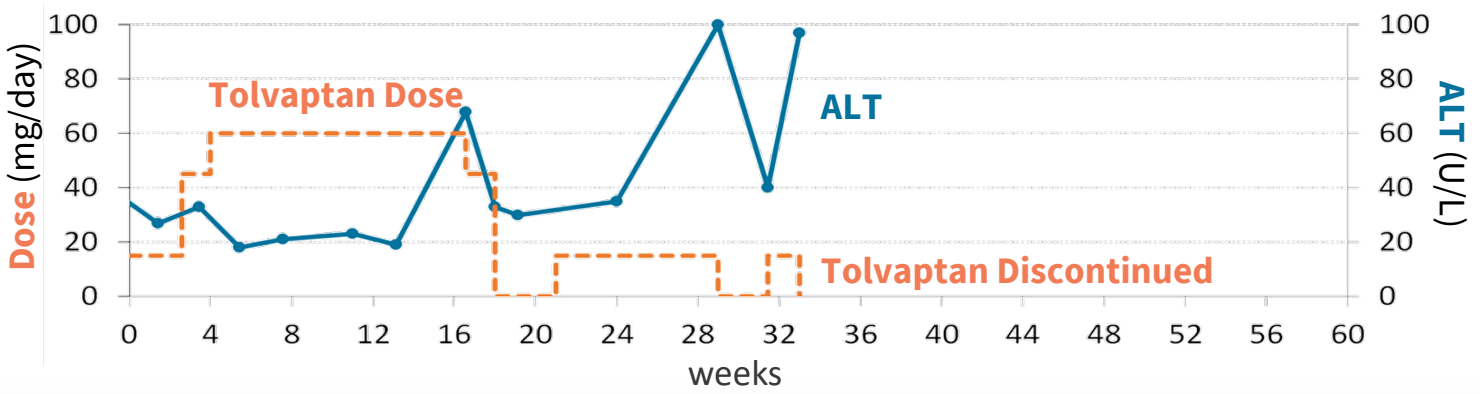
Case study: No liver toxicity observed in a tolvaptan-intolerant patient treated with lixivaptan

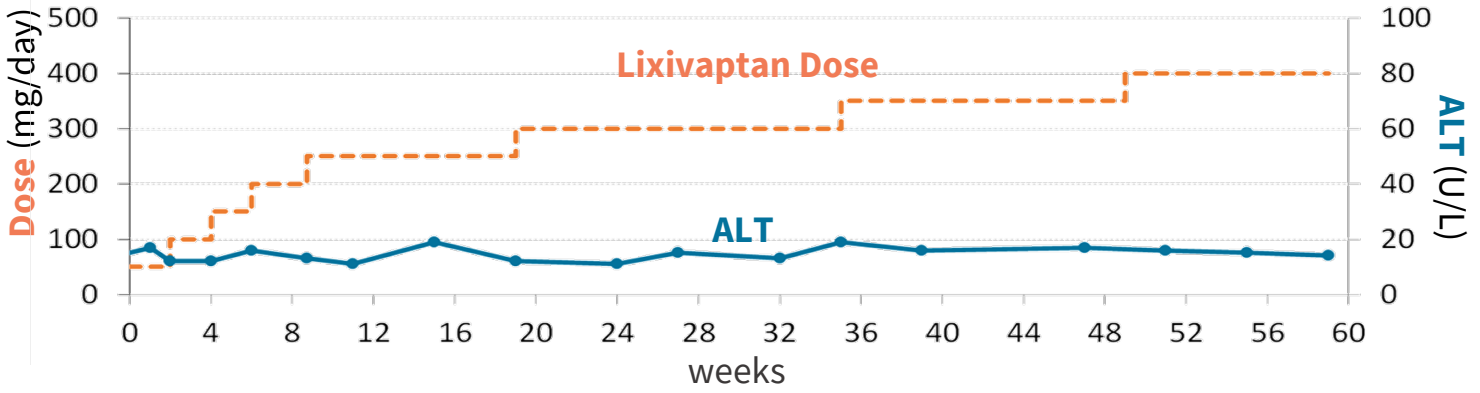
Initial tolvaptan experience

Young subject with ADPKD developed DILI on each of three unsuccessful attempts to initiate tolvaptan.



Subsequent lixivaptan experience

Lixivaptan did <u>not</u> cause any signs of liver toxicity in this highly susceptible patient during *14* months of therapy.



Four additional tolvaptan-intolerant subjects have now been successfully dosed with lixivaptan with no DILI in the ALERT Study *

* ALERT is an ongoing open-label, repeat-dose study designed to assess liver & non-liver safety in subjects who previously experienced liver chemistry test abnormalities while treated with tolvaptan and permanently discontinued from the drug for that reason. NCT04152837

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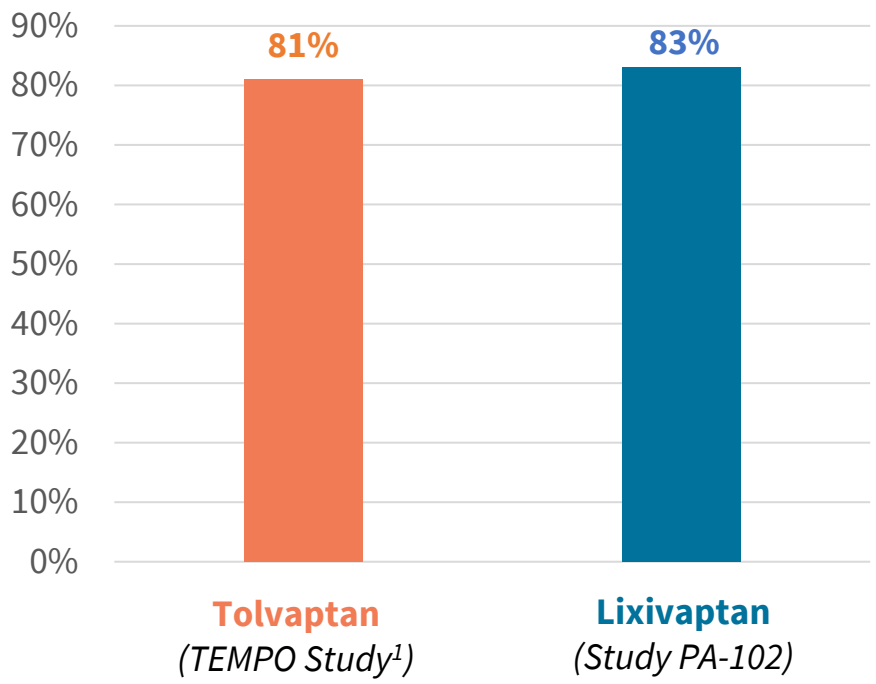
Phase 2 study showed PD comparable to tolvaptan

Share of ADPKD Patients Meeting Target Trough Uosm <300 mOsm/kg

Urine osmolality is a marker of vasopressin V2 receptor inhibition in the kidney



As expected, lixivaptan is associated with potent suppression of urine osmolality (Uosm)

1. Devuyst, Olivier, et al. "Urine osmolality, response to tolvaptan, and outcome in autosomal dominant polycystic kidney disease: results from the TEMPO 3: 4 trial." *Journal of the American Society of Nephrology* 28.5 (2017): 1592-1602.

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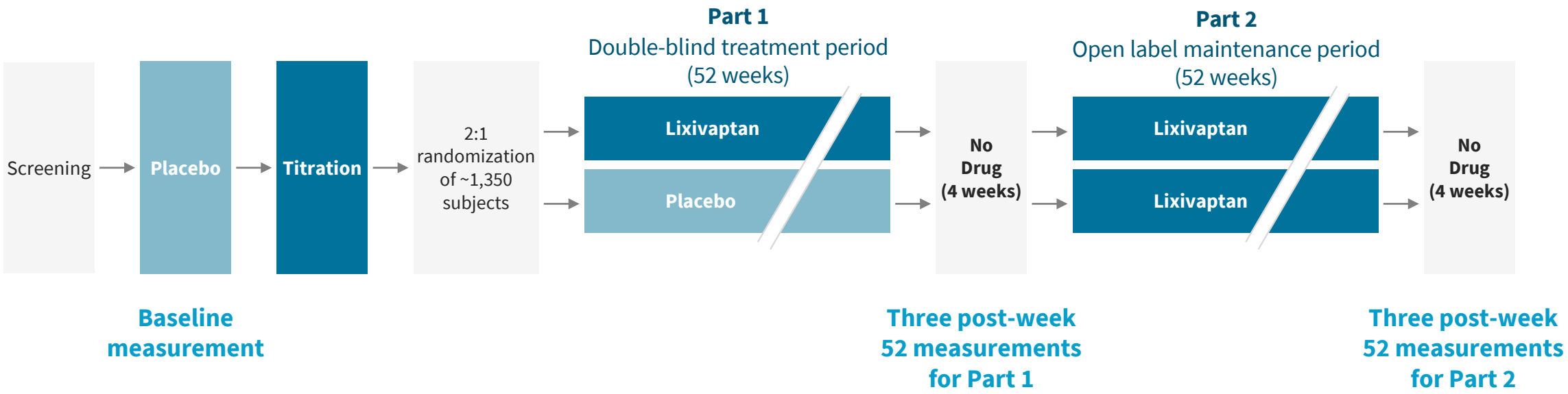
ACTION Phase 3 clinical trial design



- **Primary endpoint:** Annualized change in eGFR from baseline to end of Part 1 (post-52 weeks)
- **Key secondary endpoint:** Incidence of serum ALT levels >3x ULN in participants randomized to lixivaptan compared to those randomized to placebo in Part 1

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Next steps

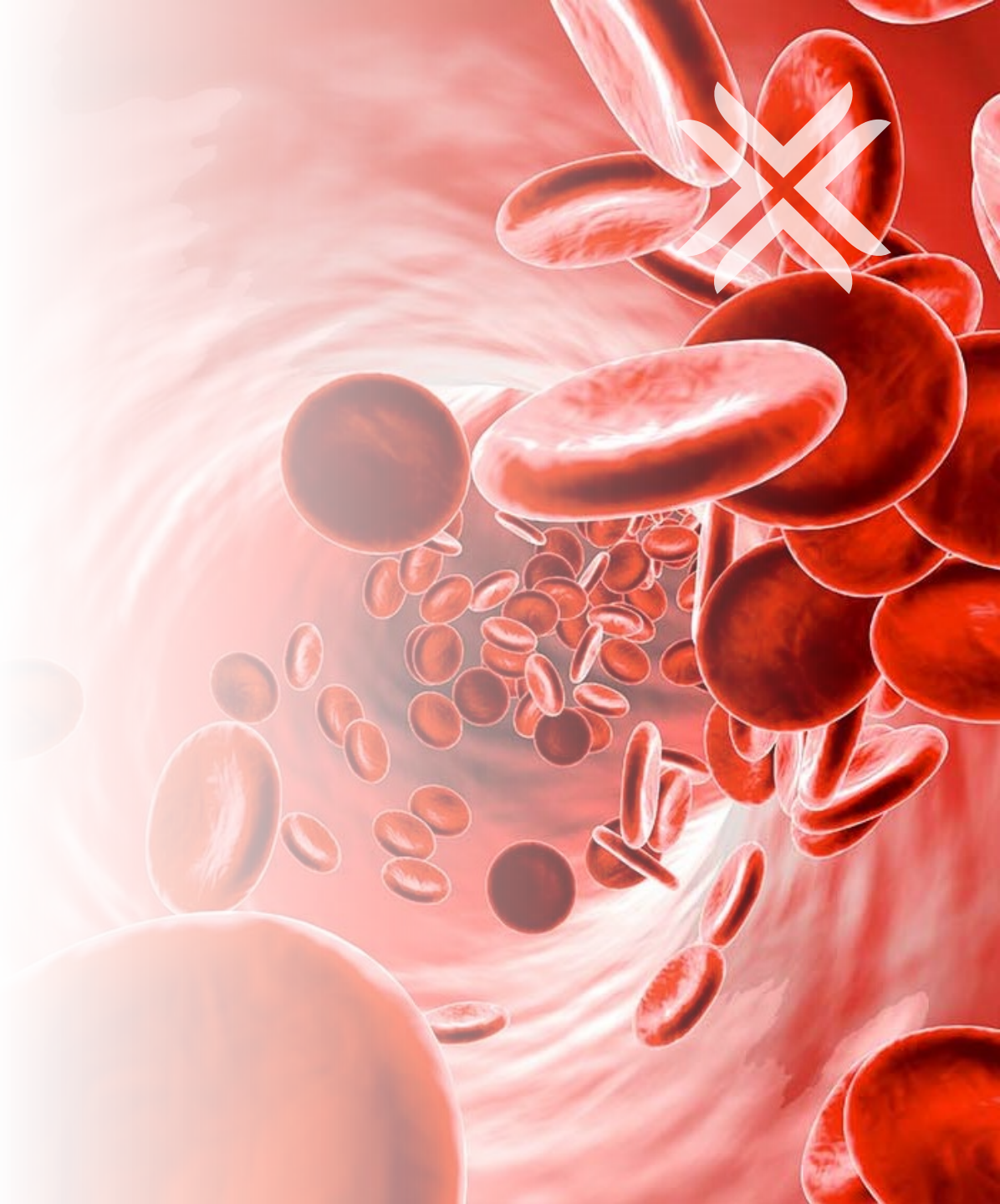
Notice of allowance granted: new patent extends protection in ADPKD at least through 2038

- Dose first subject in the ACTION Phase 3 study in 1Q22
- Target completing enrollment in the ACTION Phase 3 study by 2H 2023
- Plans to submit NDA based on one-year data from Part 1 *(pending positive data)*

PATH FORWARD

ApcinteX

SerpinPC



Differentiation

Potential benefits of SerpinPC

Novel MoA (non-factor) for **hemophilia A and B**

Compelling efficacy

Excellent safety profile without potential thrombosis

Convenient **subcutaneous administration**

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Unmet need

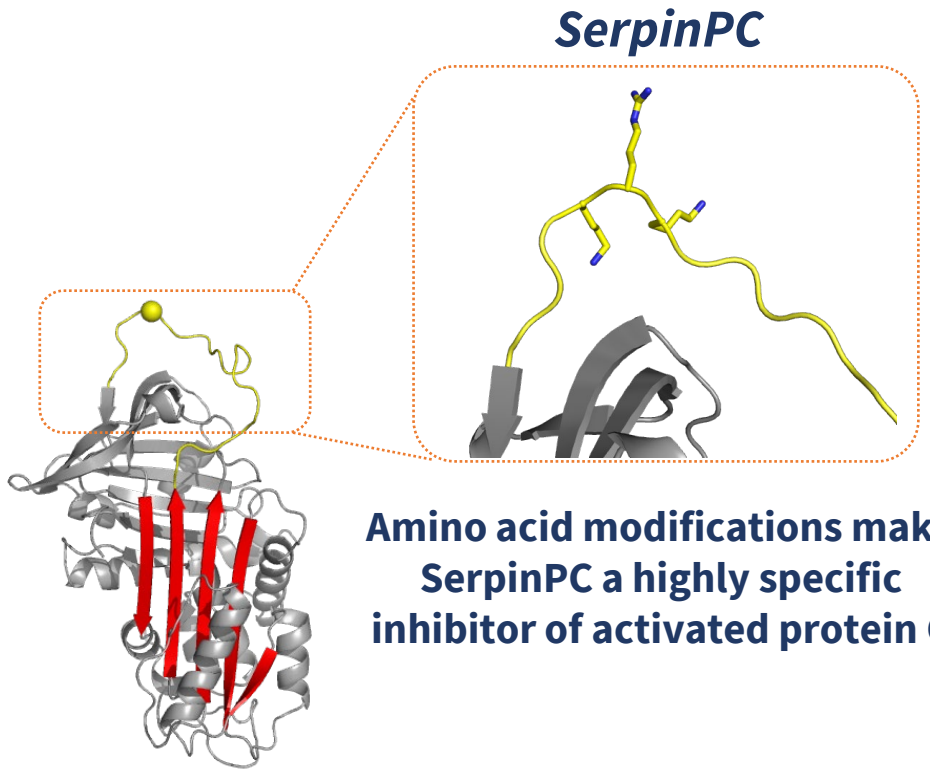
Potential “one-size-fits all” approach for both hemophilia A and hemophilia B

- **Large market opportunity: $9.6B** Hemophilia A market and **$2.1B** Hemophilia B market worldwide as of 2020[1]
- Only 20% of persons with hemophilia globally are believed to have access to adequate therapy
- SoC factor therapies require IV infusion & may be limited by inhibitory antibodies
- Only one non-factor replacement therapy is approved in Hemophilia A; none in Hemophilia B
- Need for treatment alternatives that are **safe, efficacious and convenient** (subcutaneous) without risk of thrombosis, with a more pronounced need in Hemophilia B

1. Evaluate Pharma 2020 Annual Sales Worldwide by indication

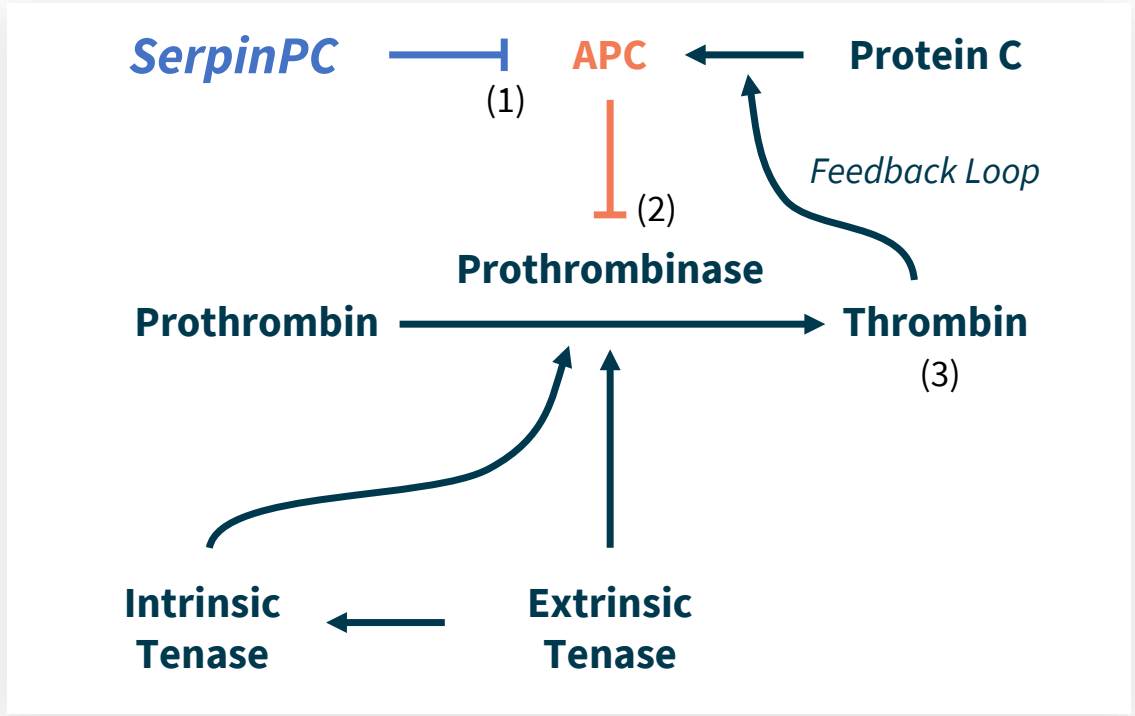
Mechanism of action (MoA)

Unique MoA, supported by human genetics based on Factor V Leiden mutation



Amino acid modifications make SerpinPC a highly specific inhibitor of activated protein C

Serpin: alpha-1-antitrypsin



SerpinPC reduces levels of circulating APC (1), thereby prolonging activity of prothrombinase (2) and directly increasing the amount of thrombin (3) at the site of tissue damage

Genetically validated target based on coinheritance of Factor V Leiden mutation with hemophilia

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Positive proof of concept data from Phase 2a

SerpinPC was observed to be well-tolerated with no evidence of thrombotic risk.

- No instances of sustained elevations in D-dimer

Improvements observed in multiple bleeding measures

At highest dose of **1.2 mg/kg SC once monthly**:

- All bleed ABR (annual bleed rate): Median **88% reduction**
- Spontaneous joint bleed ABR: Median **94% reduction**
- Zero target joints* at end of treatment period: **6 of 8 subjects**
- Zero or one bleeds during assessment period**: **5 of 8 subjects**
- Zero visible bleeds during the assessment period**: **8 of 8 subjects**

Note: all bleeding events are self reported
* Target joint = joint with >3 bleeds in any 6-month period
** Pre-specified assessment period: second half of treatment (weeks 13-24)

All subjects who successfully completed Phase 2a have enrolled in the ongoing open-label extension study

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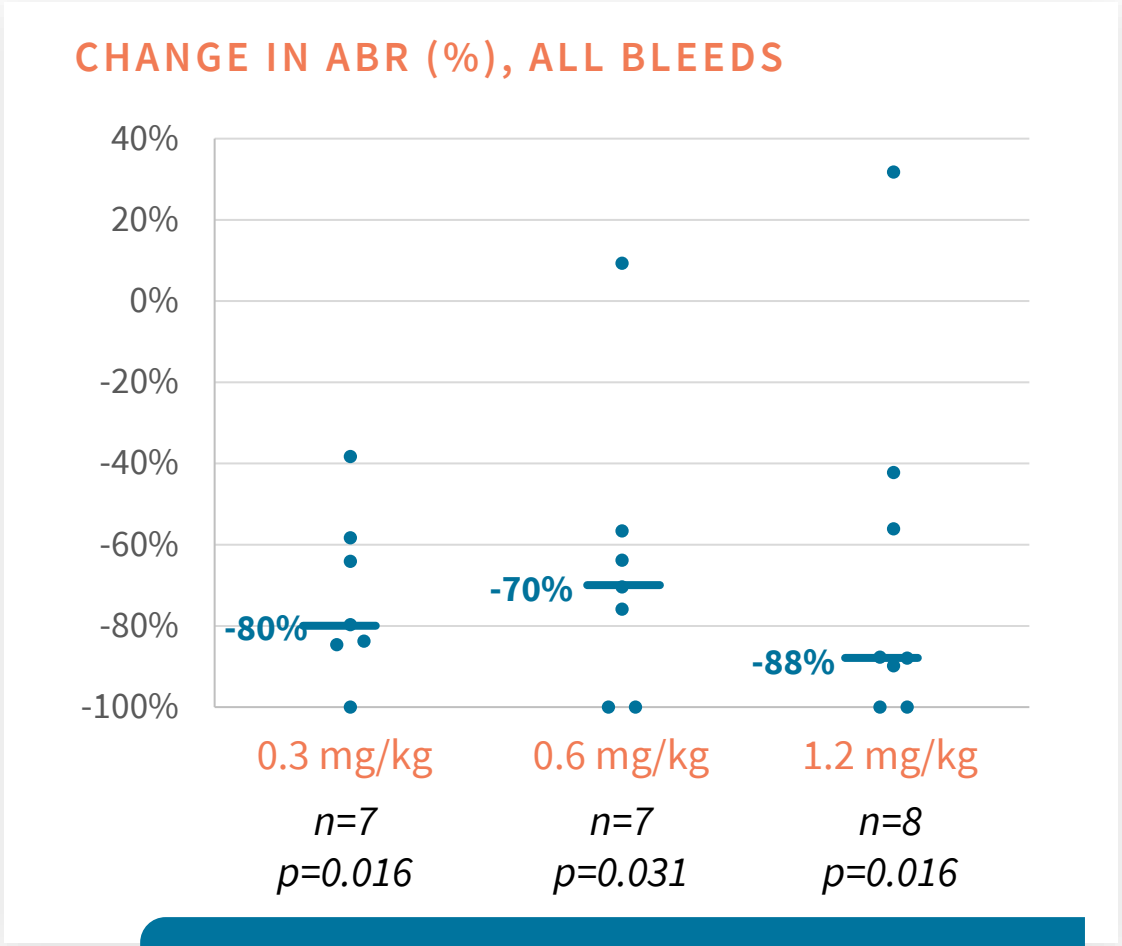
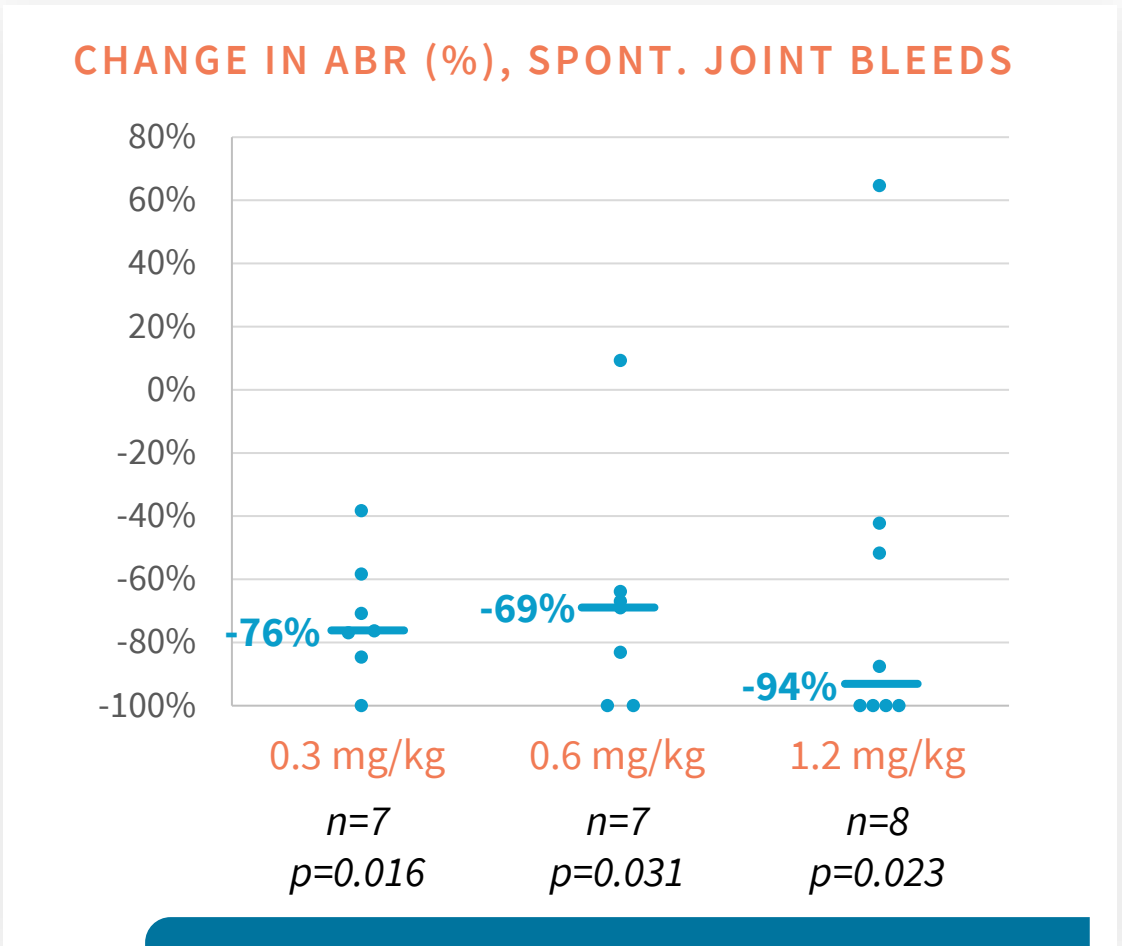
Median 88% reduction in ABR for all bleeds and median 94% for spontaneous joint bleeds at 1.2 mg/kg



At highest dose of 1.2 mg/kg, median all bleeds ABR reduced from **36.0 to 4.4**



At highest dose of 1.2 mg/kg, median spont. joint bleeds ABR reduced from **21.1 to 2.2**

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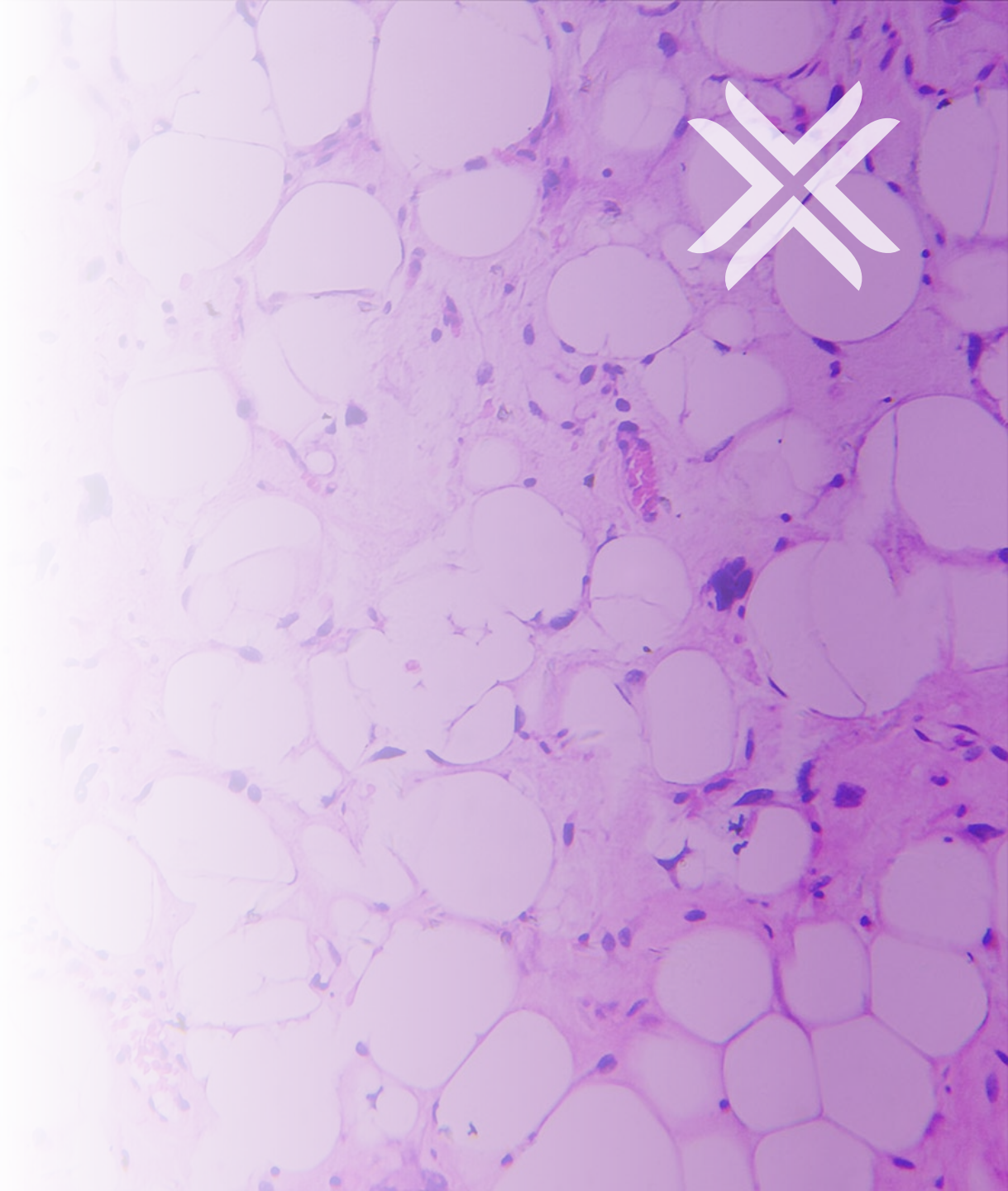
Next steps

- FDA meeting in 1Q 2022 to discuss pivotal program
- Launch global full development plan in 2022 aimed at one or more registrations
- High-dose OLE data in 2H 2022

PATH FORWARD

Z Factor

ZF874



Differentiation

Potential benefits of ZF874

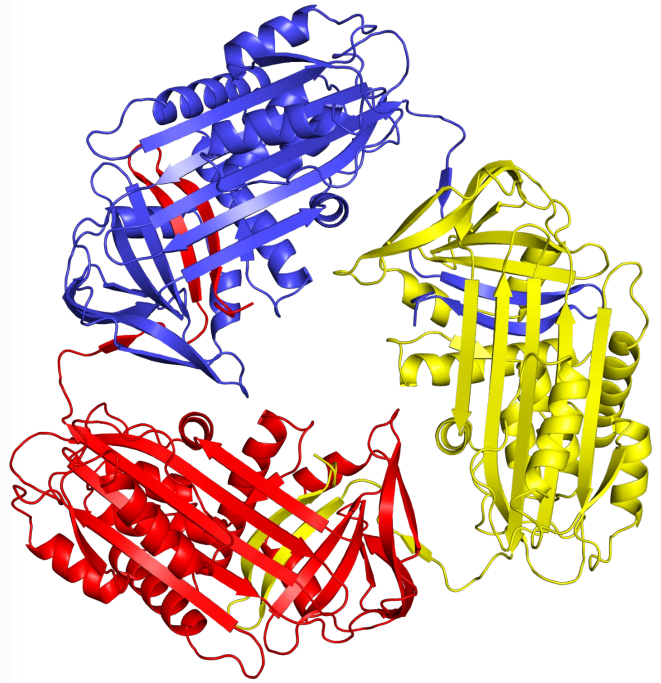
Potential to **increase functional A1AT levels** to protect the lung

Potential to **clear polymers** from the liver

Possibility to **prevent** in addition to treat disease

Introduction to Lead A1AT Folding Corrector (ZF874)

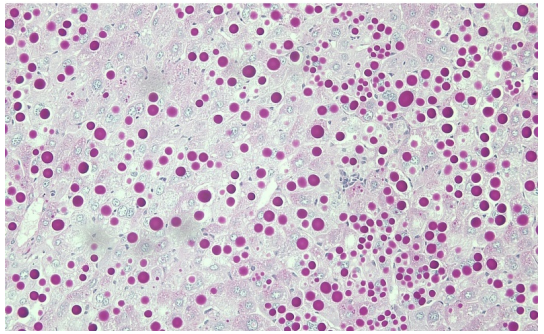
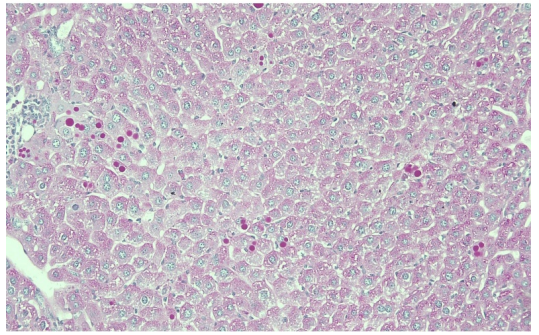
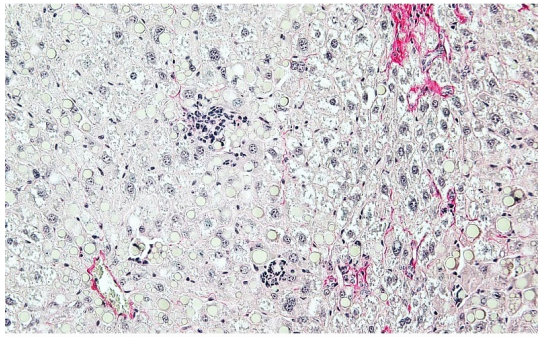
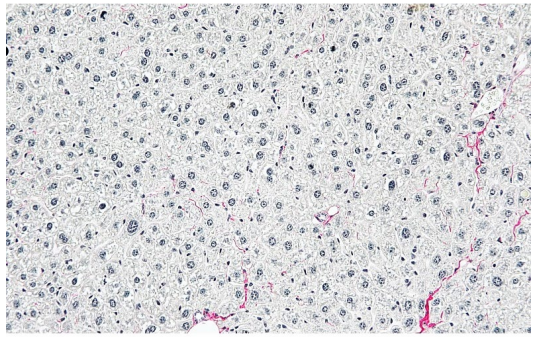
- **Small molecule folding corrector** of the Z variant of A1AT (Z-A1AT)
- **Catalytic**, non-covalent and orally bioavailable
- Discovery based on insights from a **proprietary crystal structure** of a Z-A1AT polymer
- Designed to bind to stalled folding intermediate **specific to Z-A1AT**
- Preclinical data showed **increased blood levels of Z-A1AT *and* clearance of Z-A1AT polymer from liver** in mice over-expressing human Z-A1AT at lower doses than in human studies



Abbreviations: Z-A1AT = alpha-1 antitrypsin with the Z mutation; M-A1AT = wild-type alpha-1 antitrypsin

Preclinical data show low doses of ZF874 clear polymer & reduce fibrosis

Liver histology from 84-day treatment of mice expressing human Z-A1AT (PiZ mice)

	Vehicle	**ZF874-treated** 54 mpk/day (HED 7 mpk/day)
Z-A1AT polymer (PAS-D staining)		
Fibrosis (Sirius Red staining)		

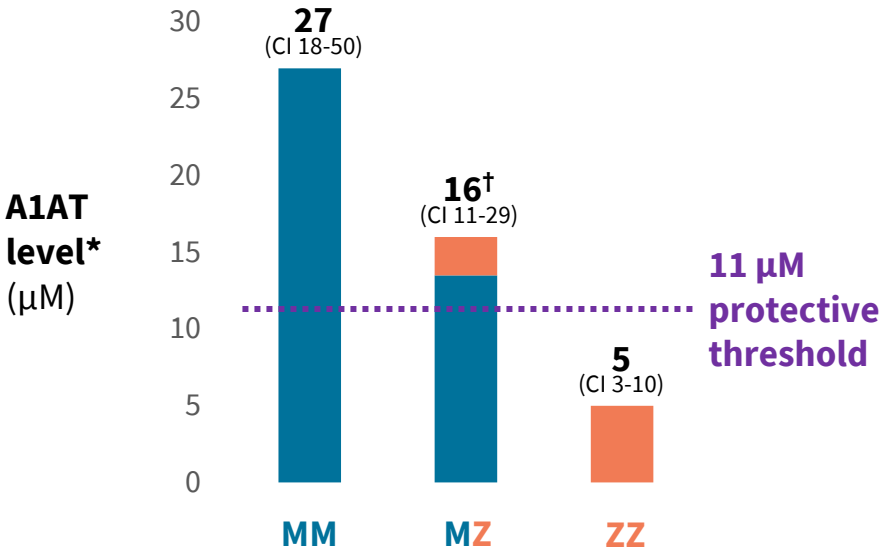
Abbreviations: mpk = milligrams per kilogram; PAS-D = Periodic Acid-Schiff staining with diastase; HED = human equivalent dose

A1AT levels for different genotypes and conceptual target for an effective folding corrector

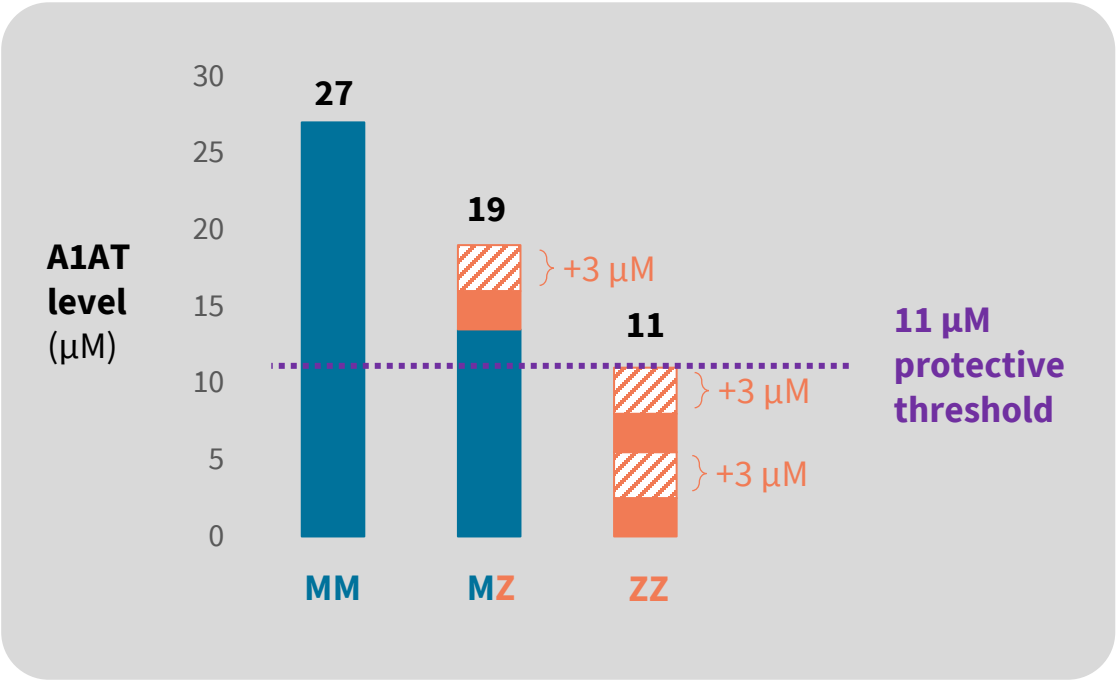
Expected level produced by M allele
Expected level produced by Z allele
Conceptual increase from treatment

Published median A1AT level by genotype

Historical based on 21,444 samples



Conceptual target: increase of 3 µM *per gene copy* to achieve 11 µM protective threshold



* Median level from Donato et al. 95% confidence intervals shown.

† M level estimated as half of MM and Z level estimated as half of ZZ

Source: A1AT levels - Donato et al. "Reference and Interpretive Ranges for α_1-Antitrypsin Quantitation by Phenotype in Adult and Pediatric Populations, *Am. J. Clin. Pathol.* 2012; 138:398-405; Protective threshold as basis for replacement therapy – Wewers et al. "Replacement Therapy for Alpha 1 – Antitrypsin Deficiency Associated with Emphysema, *NEJM; 1987 316:1055-1062*

Abbreviations: CI = confidence interval; MM = genotype with two wild-type alleles of A1AT; MZ = genotype with one wild-type and one Z mutant allele of A1AT; ZZ = genotype with two Z mutant alleles of A1AT

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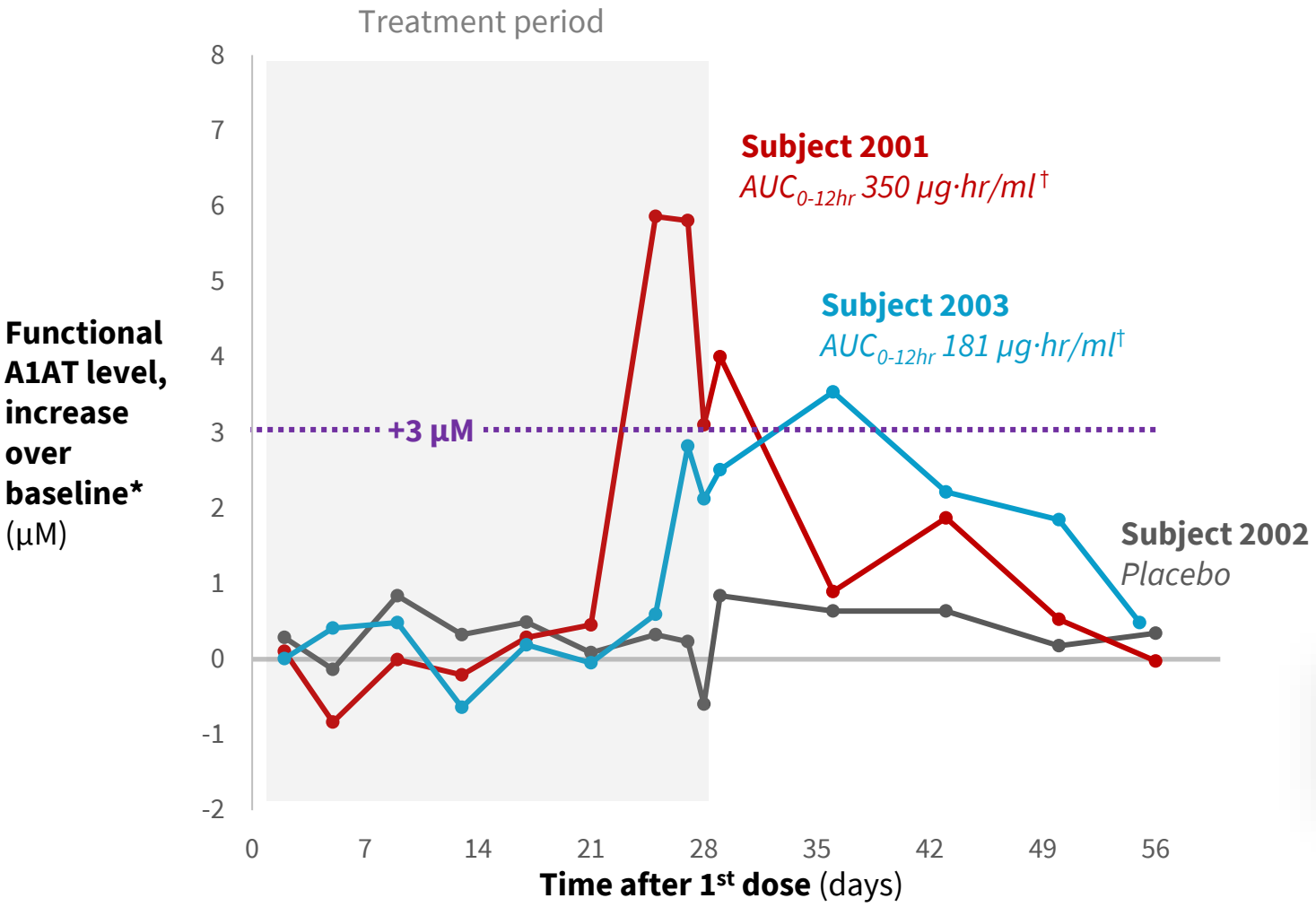
Change in A1AT functional activity for three PiMZ subjects dosed with placebo or ZF874 15 mpk BID



Demographics

First 3 subjects in Part B

Subj.	Treatment	Age	Sex	Genotype	Baseline A1AT*
2001	15 mpk BID (1.6 g BID)	47	M	MZ	17.6 µM
2002	Placebo (N/A)	23	M	MZ	12.7 µM
2003	15 mpk BID (1.1 g BID)	47	F	MZ	14.8 µM

Magnitude of response consistent with feasibility of achieving >11 µM in PiZZ subjects

* Activity level equivalent to molar amount of M A1AT reference standard. Baseline for each subject = average of Pre-Screen , Day -1, and Day 1 Pre-Dose values for each subject

† Trapezoidal AUC for the first 12 hours after the first dose on Day 28

* Baseline = average of Pre-Screen, Day -1 and Day 1 Pre-Dose values from A1AT functional assay

Abbreviations: AUC = area under the curve

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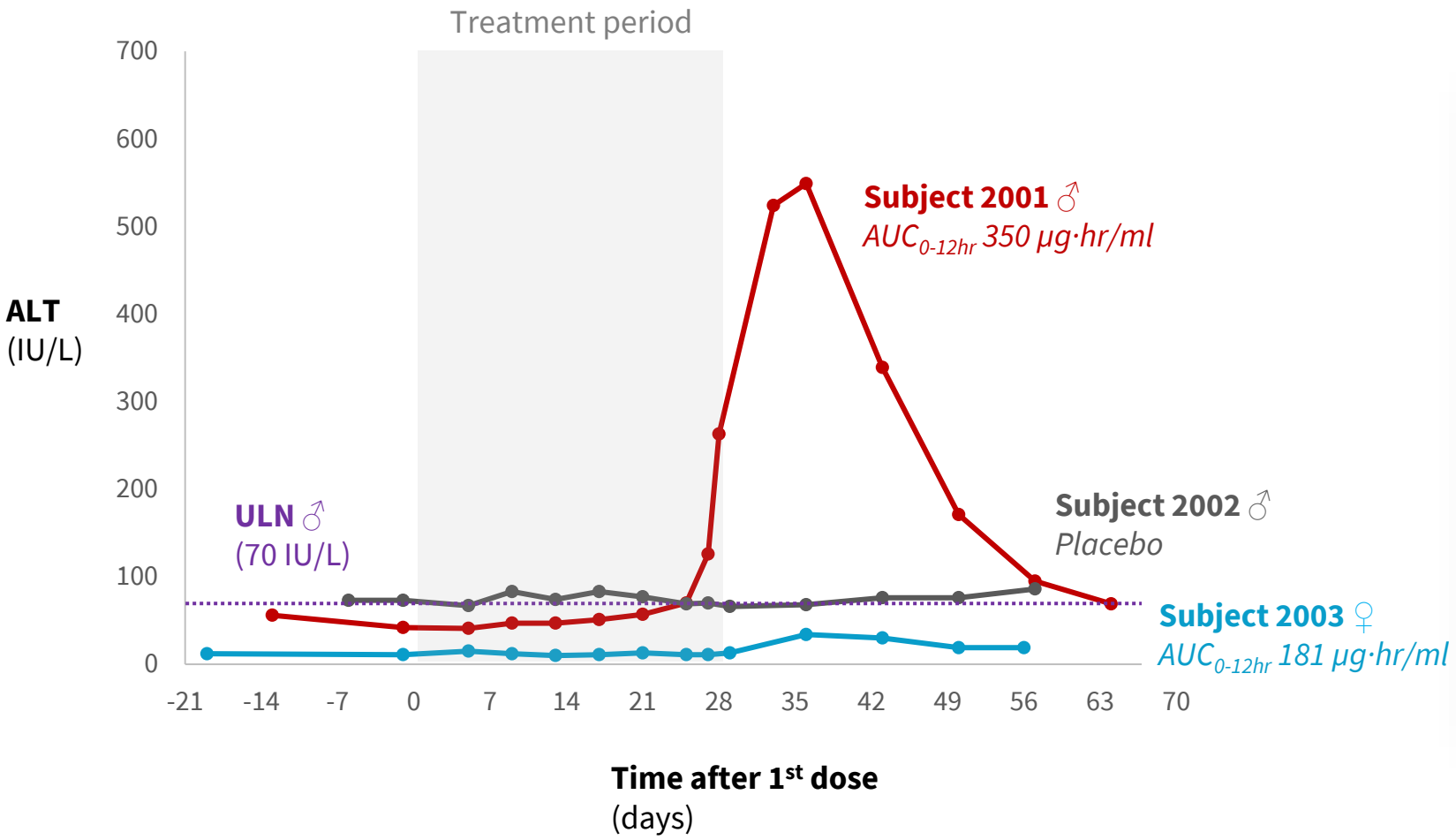
Liver signal in one PiMZ subject with highest exposure in Part B

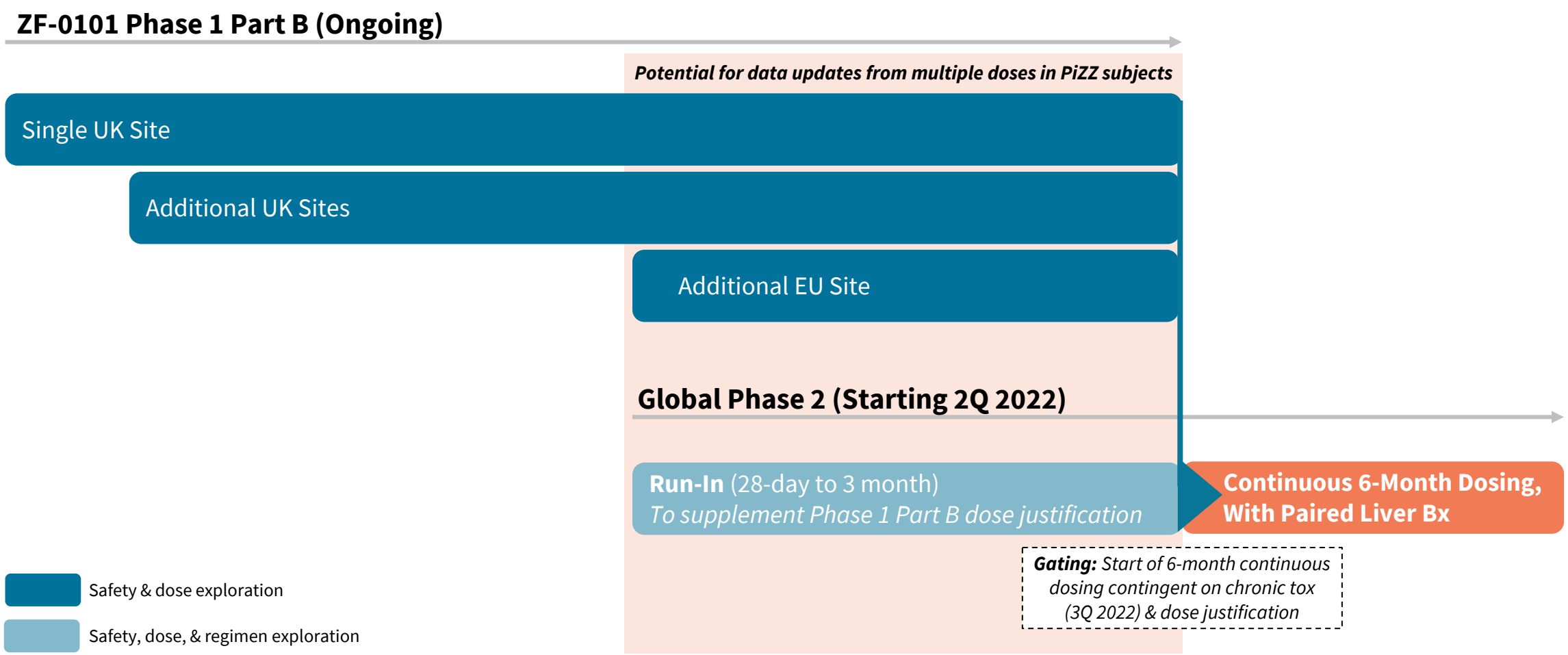


- Subject 2001 showed increases in ALT (8X ULN) and AST (3.5X ULN) after the treatment period
- In the same subject, BILI, GGT and ALP stayed in the reference range throughout the observation period
- No liver signal was observed in SAD with PiMM healthy volunteers in Part A (n = 42, dose range 1.5 mpk to 50 mpk)
- All other observed AEs were mild

* ULN ♀ (33 IU/L)
† Trapezoidal AUC for the first 12 hours after the first dose on Day 28

Abbreviations: ULN = upper limit of normal; IU/L = international units per liter; BILI = bilirubin; GGT = gamma-glutamyl transferase; ALP = alkaline phosphatase

Integrated plan to identify dose and regimen before six-month Phase 2 study



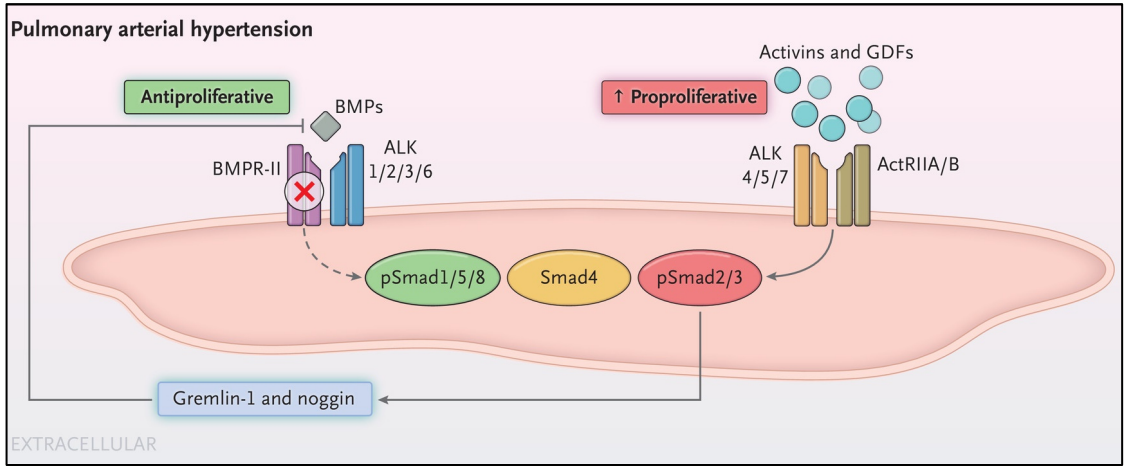
Next steps

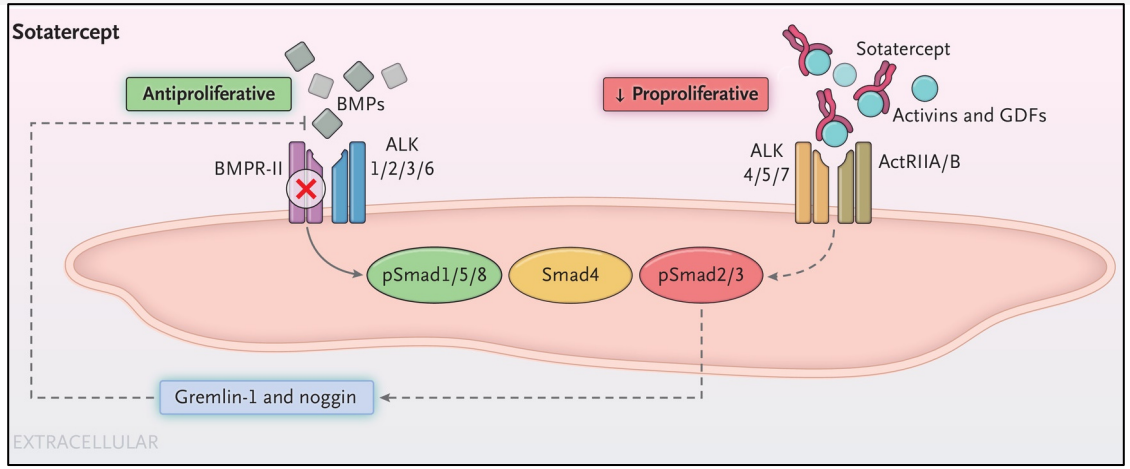
- Expand Phase 1 Part B study for further dose exploration (expect to report on PiZZ subjects in 2022)
- Start global Phase 2 study in 2Q 2022 with run-in phase

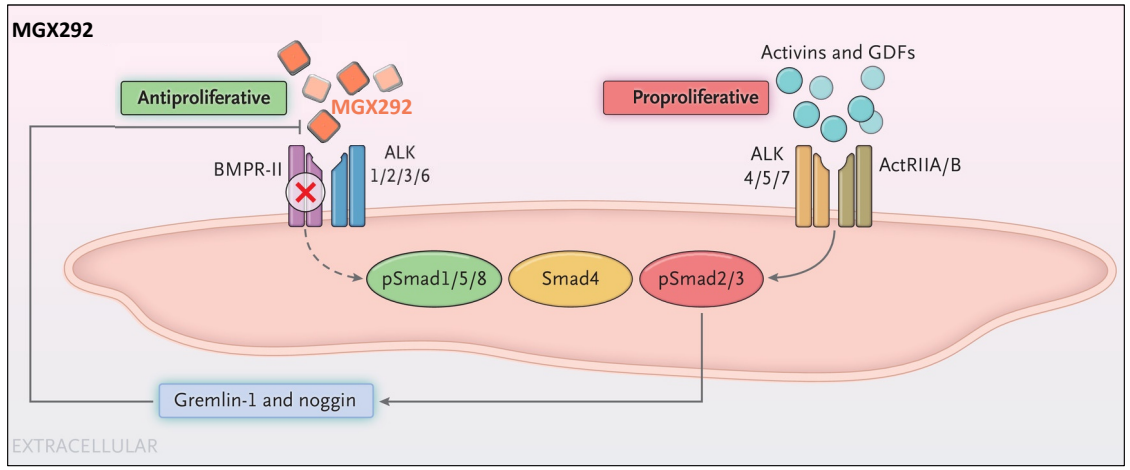
PATH FORWARD

Pre-clinical program highlights: Morphogen-IX

MGX292 activates downstream signaling in a BMPR2/ALK1 dependent manner, acting directly on genetically defined causal pathway of PAH





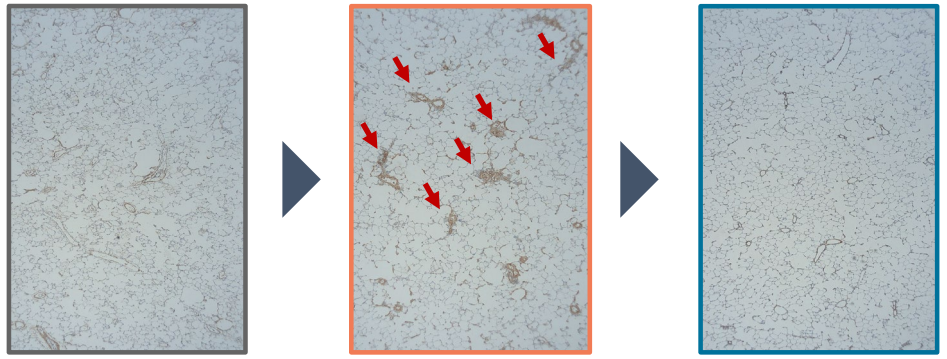


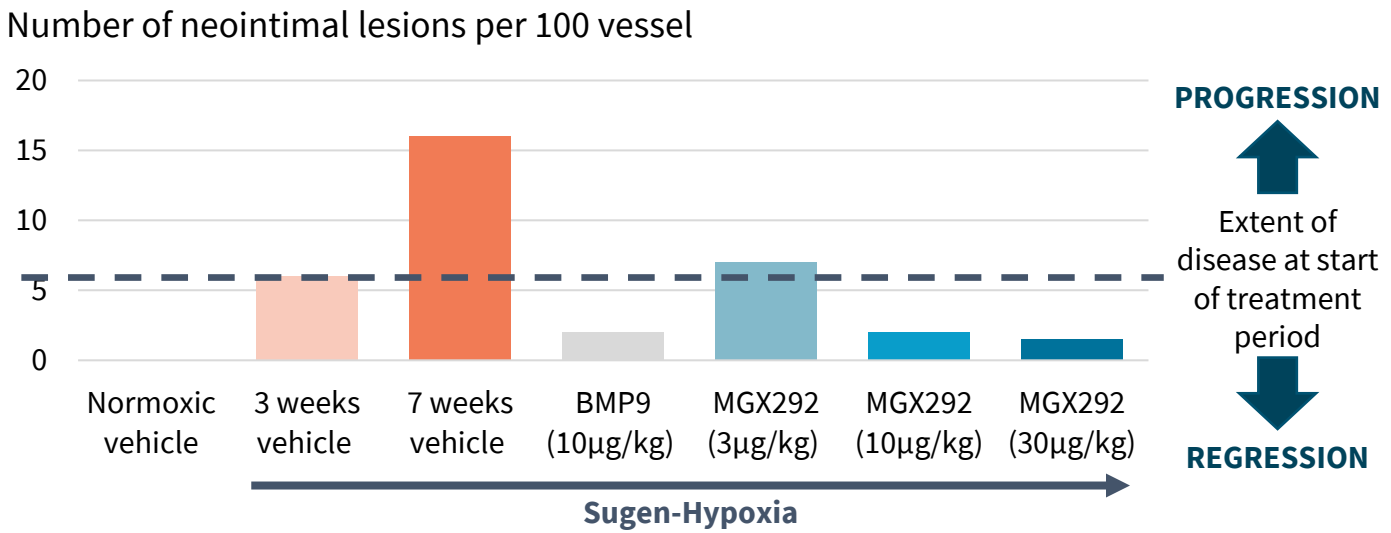
Source: Adapted from Humber et al., NEJM 2021

Pre-clinical program highlights: Morphogen-IX

- Morphogen-IX's MGX292 is a recombinant **BMP9 variant** which **directly targets the BMPR2/ALK1 pathway**
- In contrast, experimental PAH therapies inhibit Activin signaling with indirect effects on the BMPR2 pathway
- MGX292 is in the IND-enabling stage, with **IND / CTA planned for late 2022**

MGX292[1] reversed neointimal lesions in Sugen-hypoxia rat model of severe PAH





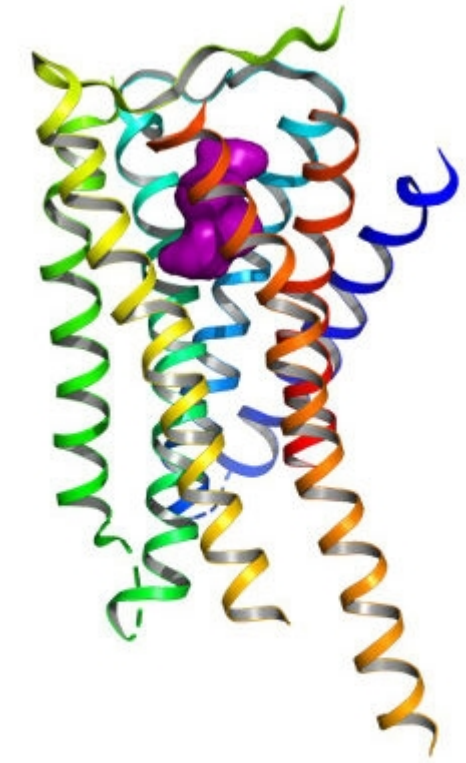
1. MGX292 treatment was given daily for 4 weeks
2. Red arrows depict vascular lesions

Pre-clinical program highlights: Orexia Therapeutics

- Potential to **address underlying disease pathology** of NT1 by re-activating orexin receptors
- **Other oral orexin agonists not far ahead:** only one in the clinic (TAK-861 in Phase 1) and one in IND-enabling studies (ALKS 2680)
- **Exclusive license to Sosei Heptares' StaR® technology** and recently announced **exclusive collaboration with Schrödinger** to support novel discovery efforts (not focused on lead programs)
- Candidate selection ongoing; **efficacy data from Phase 1 as early as 2023**

sosei HEPTARES

SCHRÖDINGER

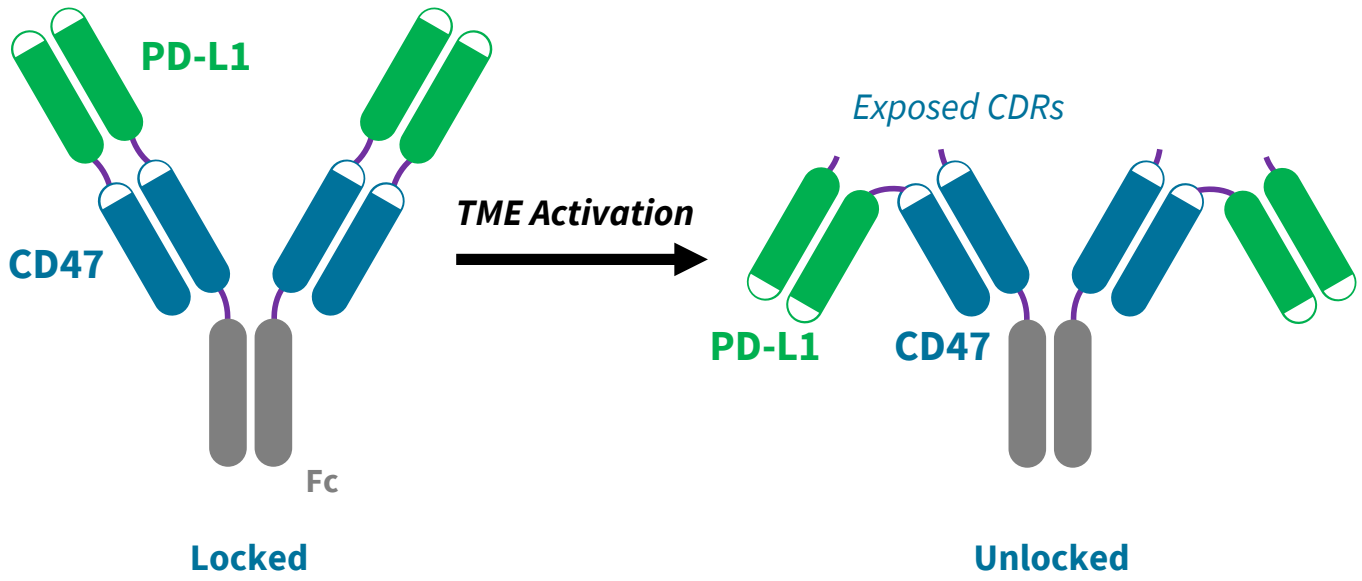


X-ray structure of OX2R with small molecule orexin agonist

CENTESSA PHARMACEUTICALS

Pre-clinical program highlights: LockBody

- **Unique LockBody® platform** has the potential to facilitate the rapid generation of a portfolio of innovative **conditional bispecific** clinical candidates
- LockBody® fixes key issue with **CD47 and CD3 bispecifics**, as cell killing is silent until "unlocked"
- Hinge cleavage in tumor micro-environment leads to **enhanced specificity/reduced toxicity**
- Candidate selection ongoing



Green: Targeting Domains, *e.g., PD-L1, PSMA*

Blue: Locked Binding Domains, *e.g., CD3, CD47, 4-1BB, CD16, CD28, CD29*

Milestones and cash runway

Upcoming catalysts

CLINICAL PROGRAMS

Ph2 study dosing commences for Pega-One's imgatuzumab in cSCC (1Q22)

Registration study initiation for ApcinteX's SerpinPC in Hemophilia A & B (2022)

Data update on high-dose OLE for ApcinteX's SerpinPC (2H22)

Data update on PiZZ subjects from ongoing Phase 1 Part B study for Z Factor's ZF874 in A1AT deficiency (2022)

Ph2 run-in study initiation for Z Factor's ZF874 (2Q22)

PRE-CLINICAL PROGRAMS

CTA submission for Capella Bioscience's anti-LIGHT mAb for IPF (1H22)

IND submission for Capella Bioscience's anti-BDCA2 mAb for Systemic Sclerosis and Lupus Erythmatosus (2H22)

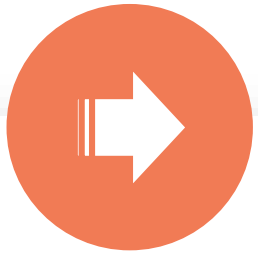
Ongoing candidate selection, IND-enabling work, and additional potential IND/CTA submissions

Projected cash runway into 2024*

* Company expects the cash and cash equivalents as of Sept 30, 2021, plus the net proceeds of the first tranche, supplemented by the additional funds available under the Oberland Facility, if drawn, to fund operations into 2024.

CENTESSA PHARMACEUTICALS

Investment highlights



Diversified pipeline

- Multiple high-value programs in rare disease and oncology
- Potential first-in-class / best-in-class assets
- Validated mechanisms and/or human genetics rationale
- Each with potential to address $1B+ markets

Novel business model

- Fueled by innovation-focused hubs led by disease-specific experts
- Driven by a centralized team of industry experts focused on long-term value creation
- Combines biotech agility with capital efficiency

Solid financials

- Cash & equivalents: $653.4m[1]
- Oberland facility: up to $225m available
- Projected cash runway into 2024[2]

Our mission: Deliver consequential medicines to patients by striving to make the unprecedented possible

1. On a pro forma basis as of September 30, 2021; inclusive of net proceeds of $74.6m from first tranche received under Oberland Agreement on October 4, 2021.
2. Cash and cash equivalents as of Sept 30, 2021, plus net proceeds of first tranche, supplemented by additional funds available under Oberland Facility, if drawn, expected to fund operations into 2024.

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