CENTESSA PHARMACEUTICALS

Corporate Overview

Asset-Centric. Patient-Centric.

December 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 does not contain all the information that is or may be material to investors or potential investors and should not be considered as advice or a recommendation to investors or potential investors in respect of the holding, purchasing or selling of securities or other financial instruments and does not take into account any investor's particular objectives, financial situation or needs. The communication of this presentation may be restricted by law; it is not intended for distribution to, or use by any person in, any jurisdiction where such distribution or use would be contrary to local law or regulation. This presentation is not directed to or intended for distribution, or transfer, either directly or indirectly to, or use by, any person or entity that is a citizen or resident or located in any locality, state, country or other jurisdiction where such distribution, transfer, publication, availability or use would be contrary to law or regulation or which would require any registration or licensing within such jurisdiction.

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 related to the Company's ability to deliver impactful medicines to patients; the ability of our key executives to drive execution of the Company's portfolio of 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; the development and therapeutic potential of our product candidates, including SerpinPC, LB101, MGX292, OX2R and our LockBody platform; 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 for our product candidates; and our anticipated cash runway. Words such as "may," "might," "will," "could," "would," "should," "expect," "intend," "plan," "objective," "anticipate," "believe," "estimate," "predict," "potential," "continue," "ongoing," "aim," "seek," and variations of these words or similar expressions are intended to identify forward-looking 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, risks related to our ability to protect and maintain our intellectual property position; business, regulatory, economic and competitive risks, uncertainties, contingencies and assumptions about the Company; risks inherent in developing products and technologies; future results from our ongoing and planned clinical trials; our ability to obtain adequate financing, including through our financing facility with Oberland, to fund our planned clinical trials and other expenses; trends in the industry; the legal and regulatory framework for the industry, including the receipt and maintenance of clearances to conduct or continue clinical testing; 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, Omicron and any other variants, geo-political risks such as the Russia-Ukraine conflict and 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. All projections, valuations and statistical analyses are provided for information purposes only. We expressly disclaim any obligation or undertaking to release publicly any updates or revisions to any forward looking statements contained herein to reflect any change in our expectations or any changes in events, conditions or circumstances on which any such statement is based, except as may be required by law. They may be based on subjective assessments and assumptions and may use one among alternative methodologies that produce different results and to the extent they are based on historical information, they should not be relied upon as an accurate prediction of future performance.

This presentation discusses product candidates that are under clinical study, and which have not yet been approved for marketing by the U.S. Food and Drug Administration or any other regulatory agency. No representation or warranty, express or implied, is made as to the safety or effectiveness of these product candidates for the use for which such product candidates are being studied. The trademarks included herein are the property of the owners thereof and are used for reference purposes only. Such use should not be construed as an endorsement of such products. Certain information contained in this presentation relates to or is based on studies, publications, surveys and other data obtained from third party sources and the Company's own internal estimates and research. While we believe these third-party sources to be reliable as of the date of this presentation, we have not independently verified, and make no representation or warranty, express or implied, as to the adequacy, fairness, accuracy or completeness of, any information obtained from third party sources. Finally, while we believe our own internal research is reliable, such research has not been verified by any independent source.

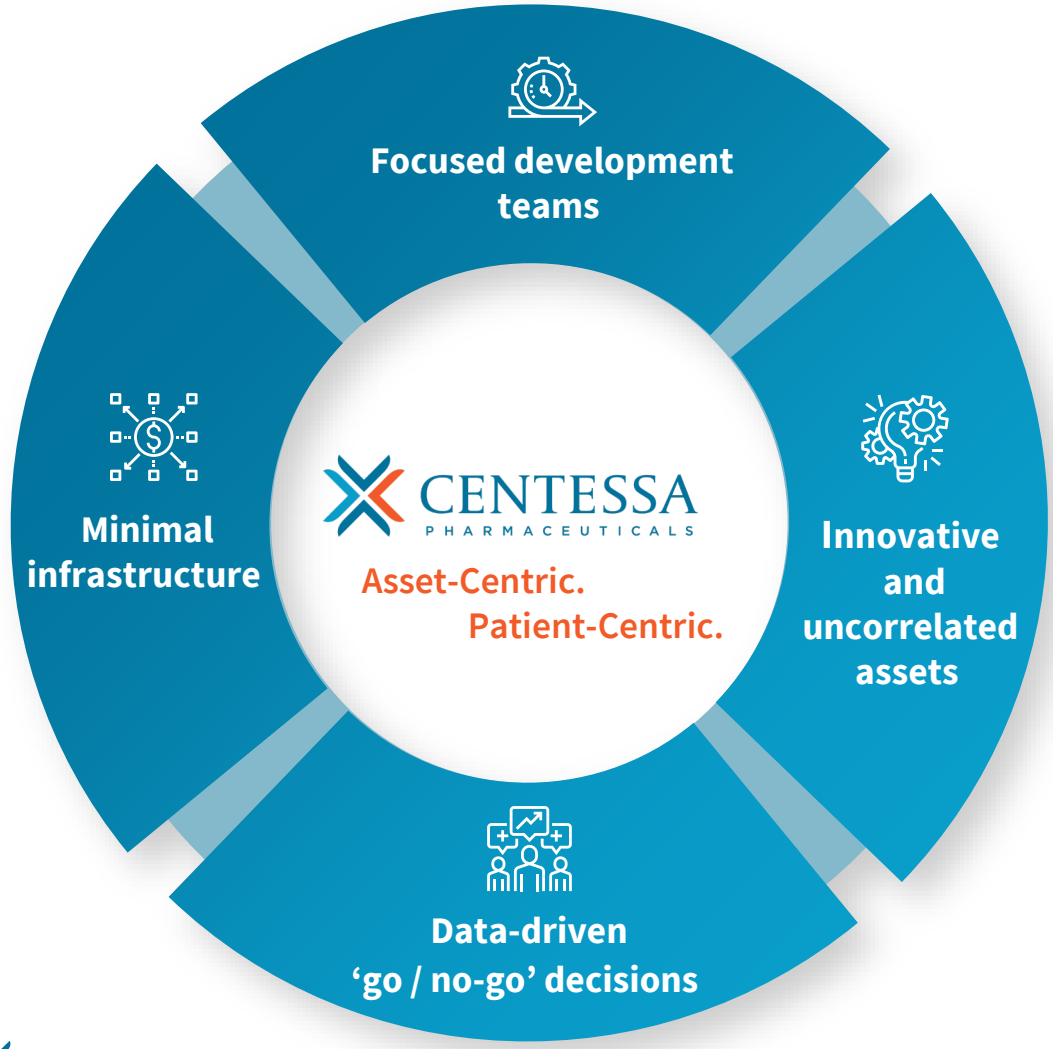
Discovering and developing medicines that are transformational for patients

- Multiple potential blockbuster assets
- Cash runway into 2026 enables clinical readouts across portfolio
- World-class R&D team

Note: **$444.8 million** in cash and cash equivalents as of September 30, 2022.

DIFFERENTIATION

We are a transformational pharmaceutical company fueling an innovative pipeline



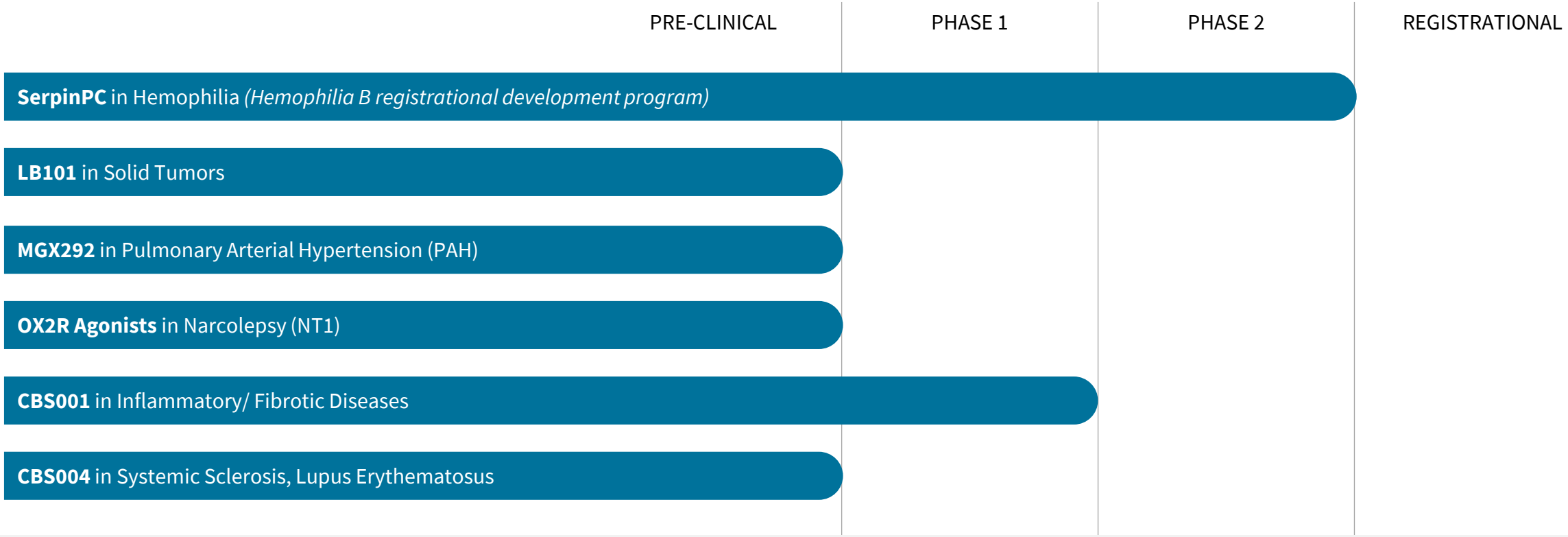
MULTIPLE PATHWAYS TO SIGNIFICANT VALUE CREATION

Lead Assets	Disease	Estimated Market Size*
SerpinPC	Hemophilia B	**$2B+**[1]
LB101	Solid Tumors	**$10B**[1]
MGX292	Pulmonary Arterial Hypertension (PAH)	**$6B**[1]
OX2R Agonists	Narcolepsy (NT1)	**$2B+**[1]

*Source: [1]Evaluate Pharma 2021 and internal estimates
Centessa has several earlier stage programs that are not reflected on this slide.

INNOVATIVE PIPELINE

Potential first-in-class/ best-in-class medicines for patients



CASH RUNWAY INTO 2026 ENABLES CLINICAL READOUTS ACROSS PIPELINE

$444.8 million in cash and cash equivalents as of September 30, 2022.

Additional LockBody® molecules, such as LB201 are being progressed toward candidate selection expected early 2023.
Centessa has several earlier stage programs that are not reflected on this slide.

LEADERSHIP

Team with deep R&D experience and focused on execution

SAURABH SAHA MD PhD

Chief Executive Officer

Bristol Myers Squibb · NOVARTIS · Delinia · ATLAS VENTURE · McKinsey&Company

ANTOINE YVER MD MSc

EVP & Chairman of Development

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

DAVID GRAINGER PhD

Chief Innovation Officer

medicxi · RxCelerate · totalscientific · Index Ventures

IQBAL HUSSAIN

General Counsel

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

GREG WEINHOFF MD MBA

Chief Financial Officer

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

TIA BUSH

Chief Quality Officer

AMGEN

DAVID CHAO PhD

Chief Administrative Officer

BIOMED VALLEY · nectagen · STOWERS INSTITUTE · McKinsey&Company · NOVARTIS

THOMAS TEMPLEMAN PhD

Chief Technology Officer

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

KAREN ANDERSON

Chief People Officer

Baxter · BAYER · Alnylam · Biogen · mimecast

JOSH HAMERMESH MBA

SVP, Business Development

gamida cell · LOCUST WALK · Infinity · molecularinsight pharmaceuticals · Pervasis · genzyme

KRISTEN SHEPPARD ESQ

SVP, Investor Relations & Corp. Comm.

Dicerna · NxSTAGE · Akebia · EQUALLOGIC · CABLETRON SYSTEMS · enterasys

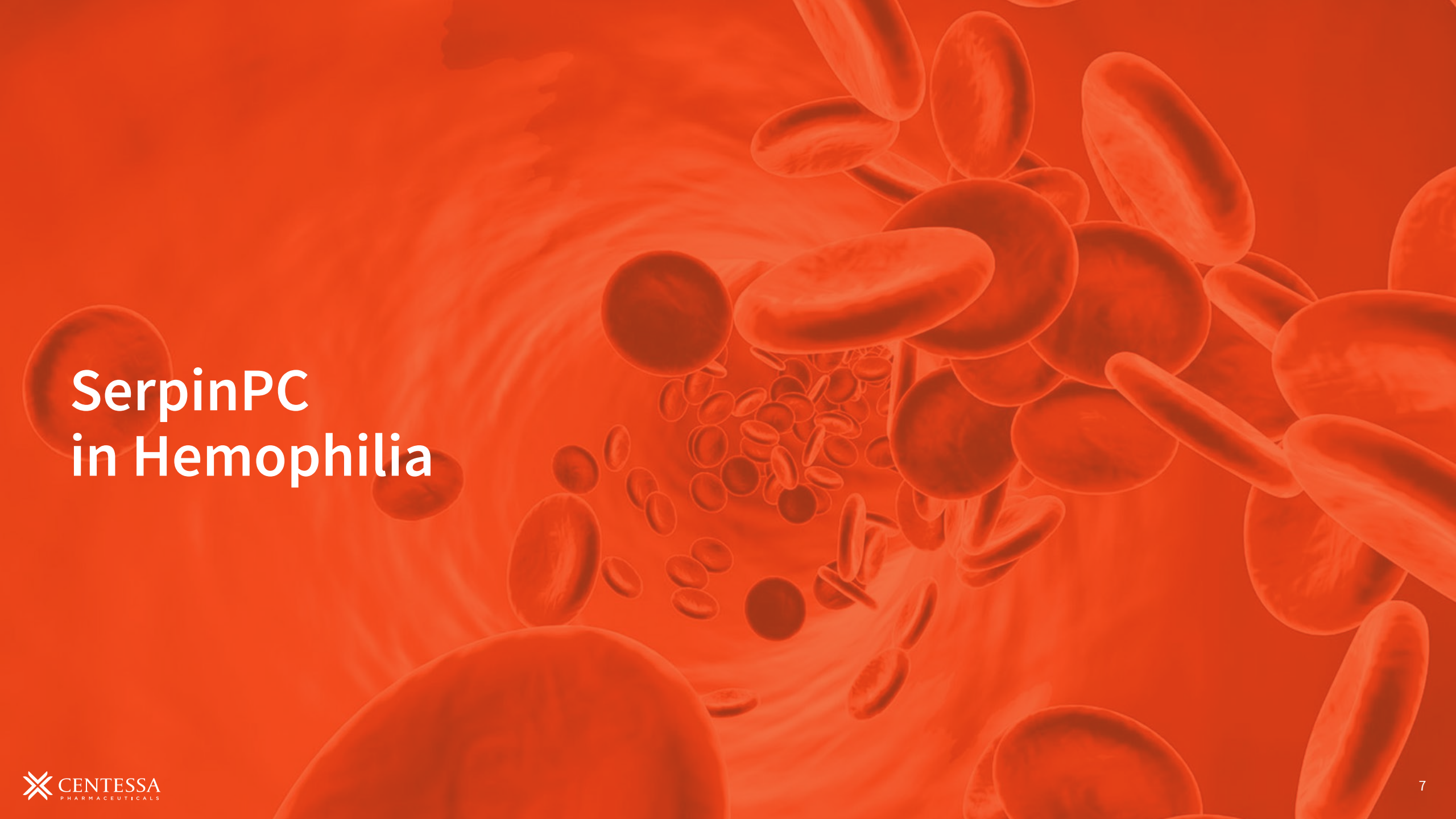
HARRIS ROTMAN PhD

SVP, Regulatory Affairs

SANOFI · Shire · Wyeth · endo · SwanBio

CENTESSA PHARMACEUTICALS

SerpinPC in Hemophilia



CENTESSA PHARMACEUTICALS

SerpinPC has potentially best-in-class attributes to address unmet need in hemophilia B

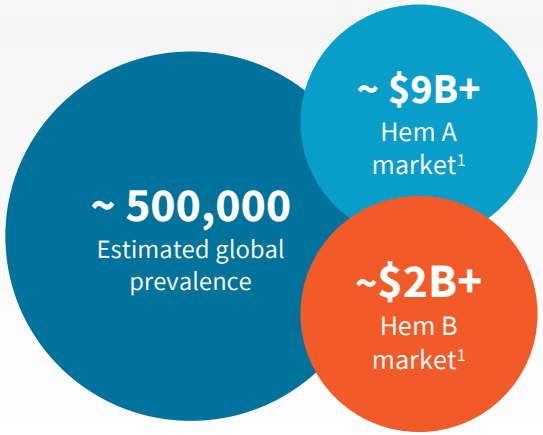
Novel MOA; designed to prevent and reduce bleeds without risk of thrombosis

HEMOPHILIA B UNMET NEED

Current hemophilia B treatments require IV infusions

Potentially competitive pipeline agents carry potential risk of thrombosis

High proportion of patients outside U.S and Europe are not treated



Novel MoA;
Showed significant **reduction in bleeding**[2]

Shown to have a **safe and well tolerated profile**[2]; **No thrombosis** observed[2]

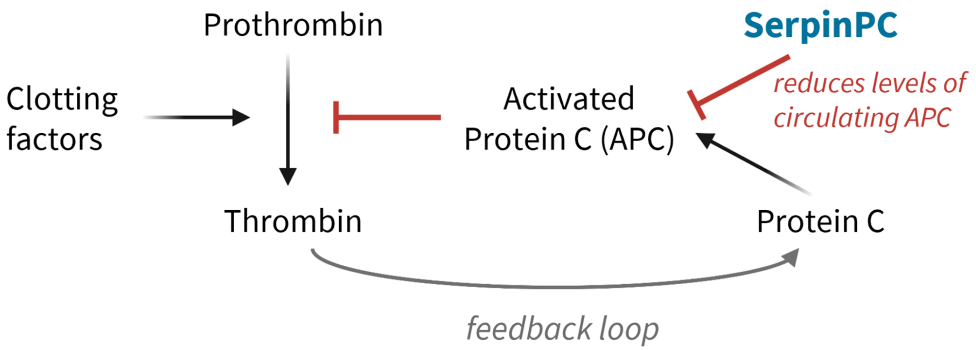
Convenient subcutaneous injection

SerpinPC is a serine protease inhibitor (SERPIN) engineered to specifically inhibit activated protein C (APC) and is being developed for the treatment of hemophilia. *Source: 1.Evaluate Pharma 2021 2. 6-month repeat-dose portion of Phase 2a Study conducted in Georgia and Moldova to evaluate safety, tolerability, pharmacokinetics and efficacy of SerpinPC in a population of severe hemophilia A and B subjects not on previous prophylaxis and with a history of frequent bleeding.

CENTESSA PHARMACEUTICALS

SerpinPC is believed to have a unique MoA supported by human genetics

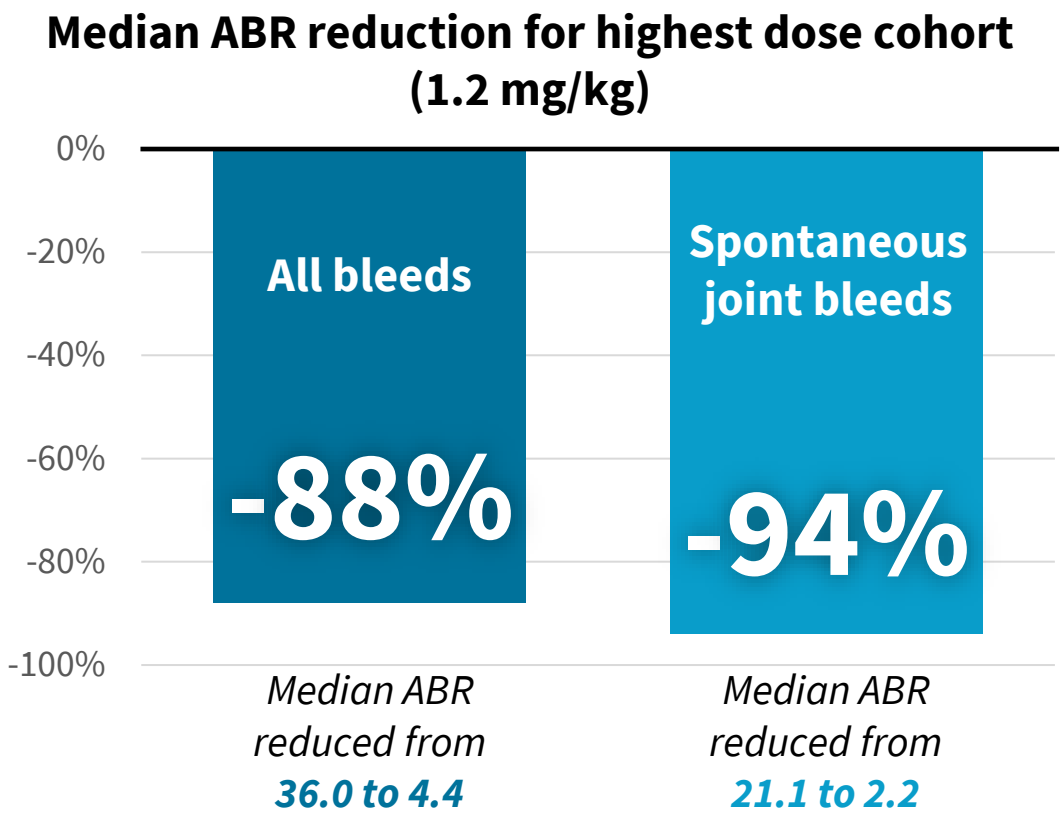
Primary APC is the target of SerpinPC



SerpinPC

- Human genetic target validation
- Engineered to specifically inhibit APC
- Inhibition of APC increases thrombin
- Feedback loop prevents excess thrombin generation

Phase 2a Study: SerpinPC showed significant reductions in bleeding rates



SerpinPC was also observed to be well-tolerated

Across all dose levels:

- No thrombosis
- No instances of sustained elevations in D-dimer

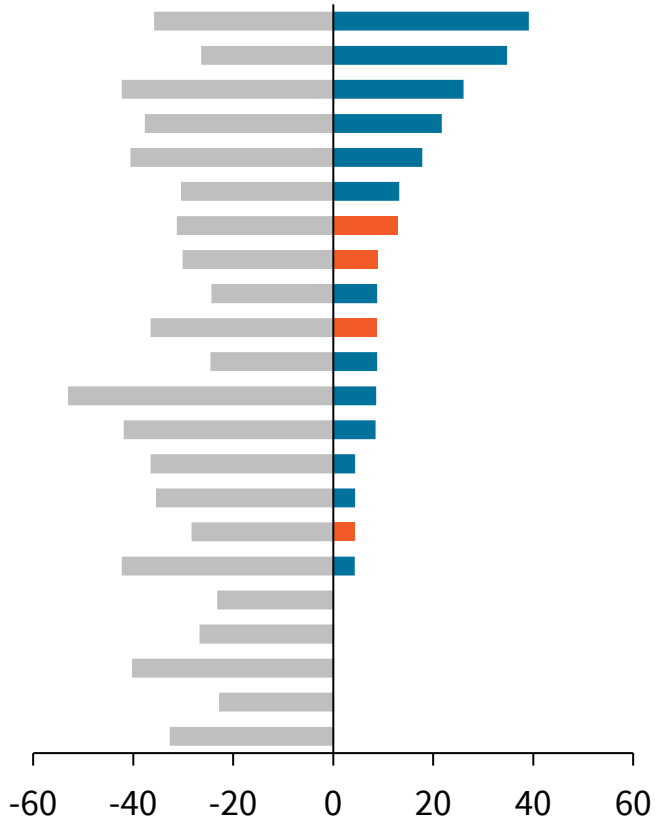
One moderate skin reaction led to withdrawal of a subject with history of a skin disorder. Two subjects with ADAs, with no apparent impact on ABRs. No other SerpinPC-related AEs.
ABR is annualized bleeding rate.
Six-month update of Phase 2a Study conducted in Georgia and Moldova to evaluate safety and efficacy of SerpinPC in a population of severe Hemophilia A and B subjects not on previous prophylaxis and with a history of substantial bleeding.

CENTESSA PHARMACEUTICALS

Phase 2a Study: Individual observed ABRs for all bleeds and spontaneous joint bleeds

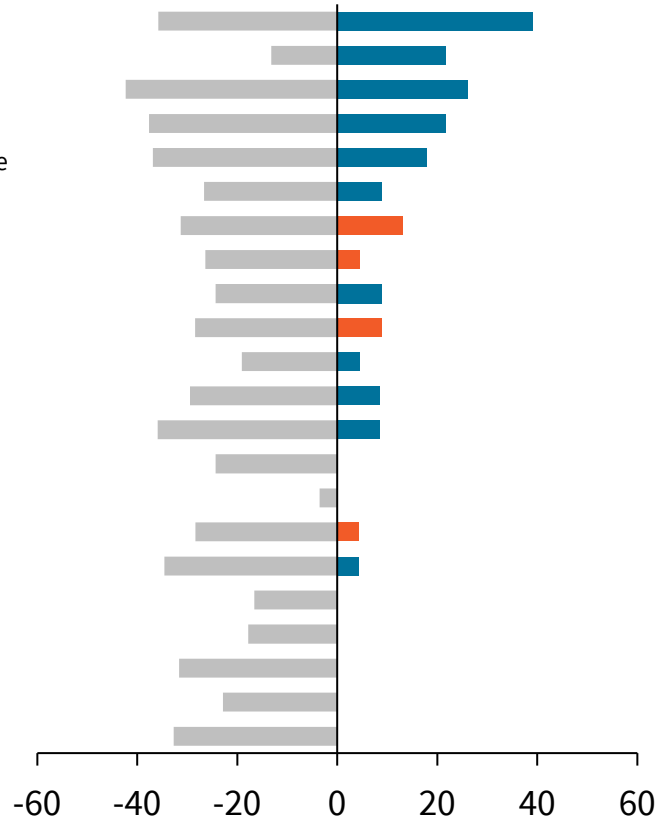
All bleeds ABR

- ABR during pre-exposure prospective observation period
- ABR on SerpinPC, Hemophilia A subjects[1]
- ABR on SerpinPC, Hemophilia B subjects[1]



Spontaneous joint bleeds ABR

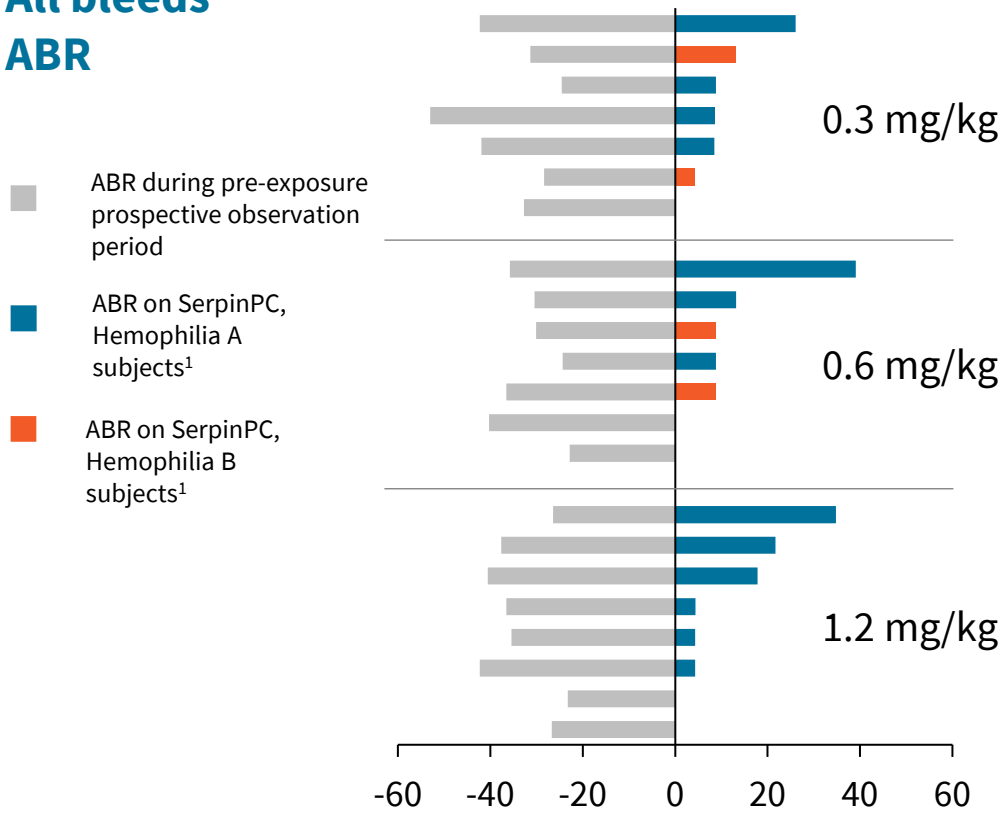
- ABR during pre-exposure prospective observation period
- ABR on SerpinPC, Hemophilia A subjects[1]
- ABR on SerpinPC, Hemophilia B subjects[1]



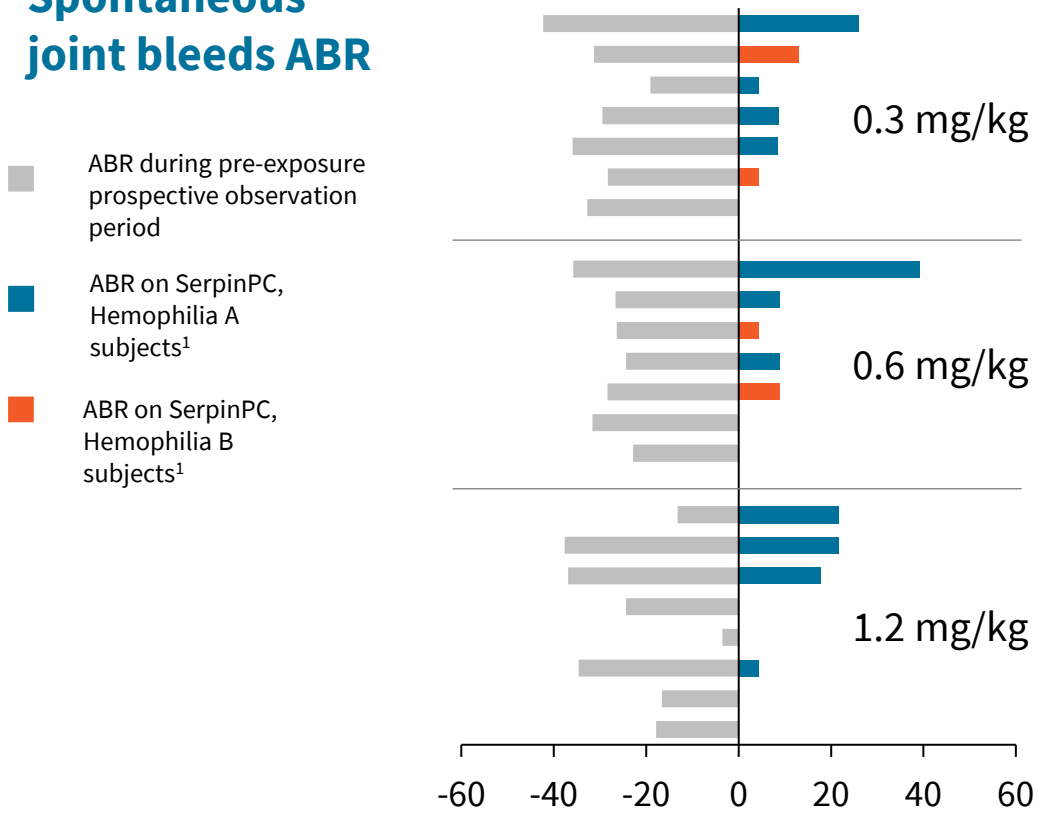
Six-month update of Phase 2a Study. ABR is annualized bleeding rate. 1. During second 12 weeks of exposure (as prespecified in the statistical analysis plan). Once monthly injections.

Phase 2a Study: Individual observed ABRs across dose cohorts

All bleeds ABR



Spontaneous joint bleeds ABR

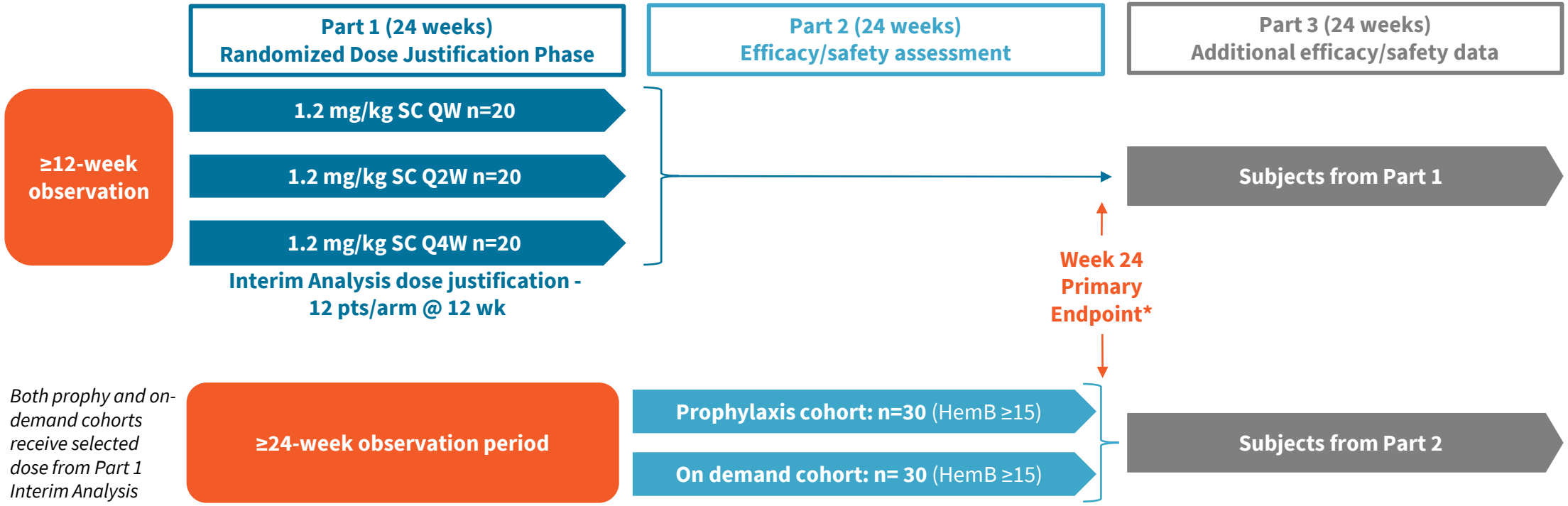


Six-month update of Phase 2a Study. ABR is annualized bleeding rate. 1. During second 12 weeks of exposure (as prespecified in the statistical analysis plan). Once monthly injections.

SerpinPC registrational development plan (Hemophilia B without inhibitors)

1 **≥12 Week Observation Study (PRESent-5):** *Designed to enroll patients and prospectively establish baseline ABR before initiation of interventional studies*

2 **Hemophilia B without inhibitors (PRESent-2)** (n=120) *Study to also include hemophilia A subjects to support safety database*



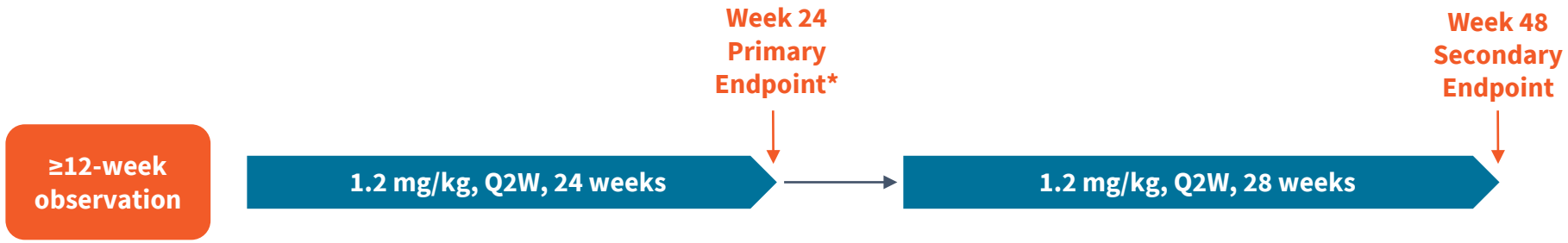
***Primary Endpoint:** Rate of treated bleeds (expressed as ABR) in the observation period and during the first 24 weeks with SerpinPC*

CENTESSA PHARMACEUTICALS

SerpinPC registrational development plan (Hemophilia B with inhibitors)

1 **≥12 Week Observation Study (PRESent-5):** *Designed to enroll patients and prospectively establish baseline ABR before initiation of interventional studies*

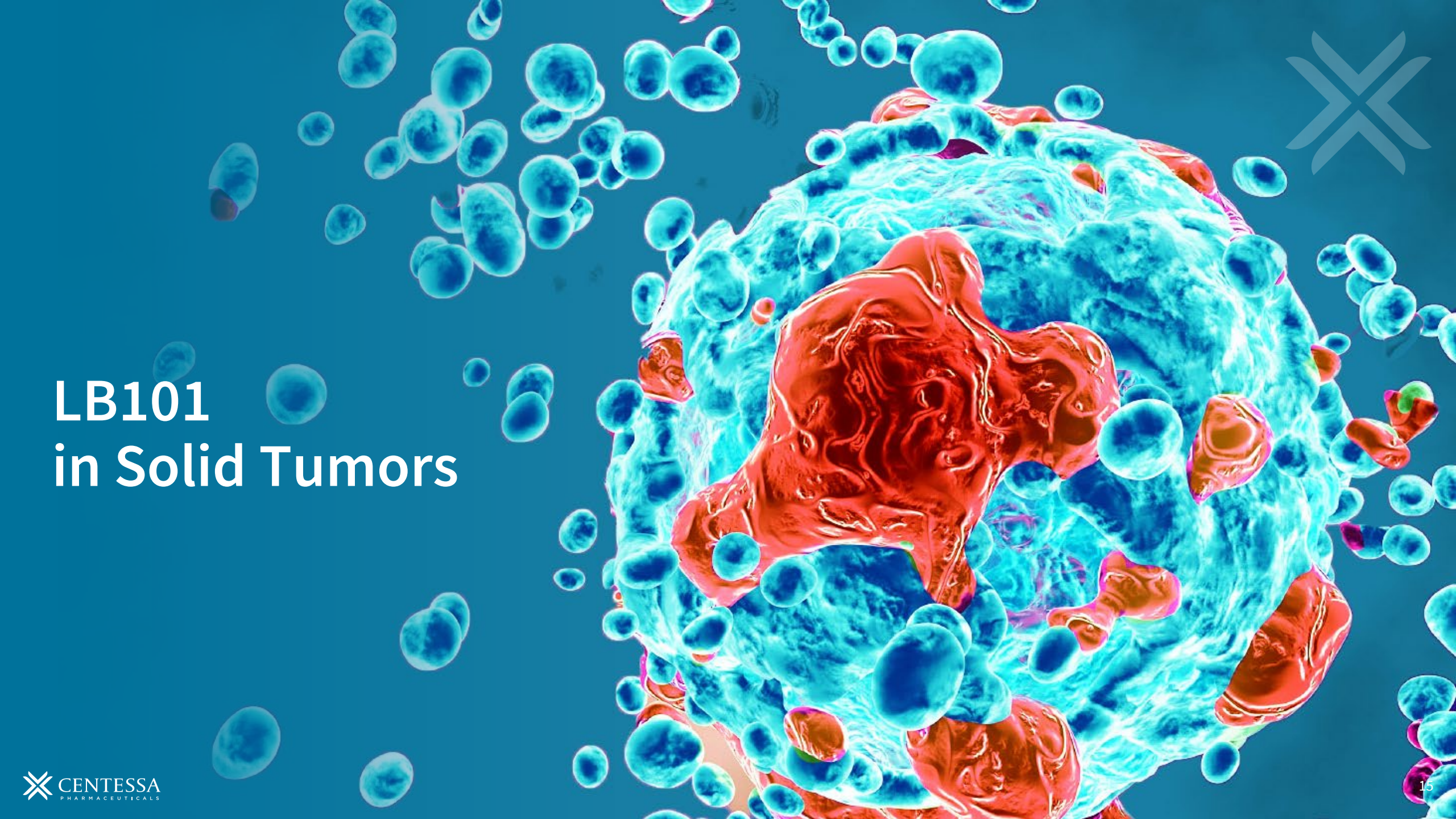
3 **Hemophilia B with inhibitors (PRESent-3)** (n<20)



***Primary Endpoint:** Rate of treated bleeds (expressed as ABR) in the observation period and during the first 24 weeks with SerpinPC*

CENTESSA PHARMACEUTICALS

LB101 in Solid Tumors



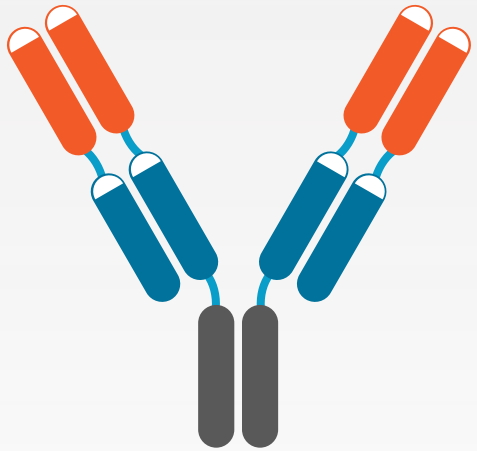
CENTESSA PHARMACEUTICALS

LB101: Potential first-in-class immunotherapy targeting solid tumors

A conditionally tetravalent PD-L1xCD47 bispecific monoclonal antibody

LockBody®

"It's all about the hinge"



Novel pharmacology focused on human IgG-derived hinges susceptible to natural intra-tumoral hinge cleavage

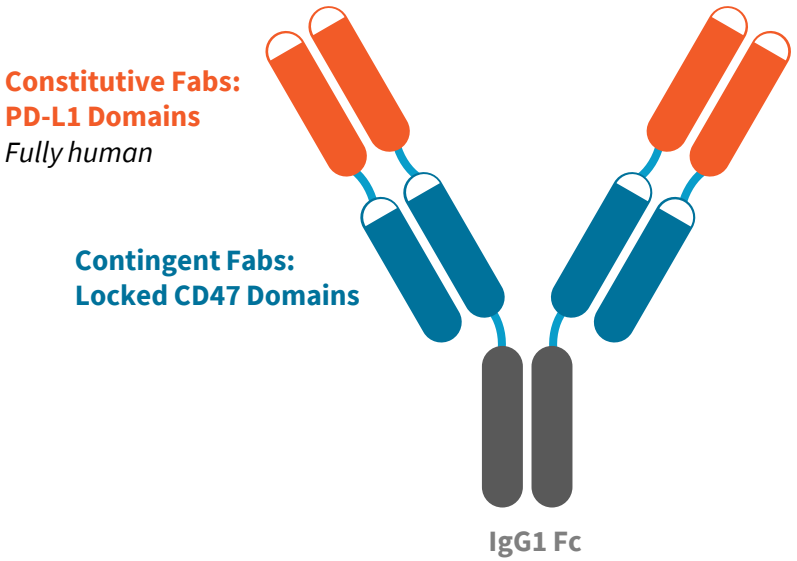
Designed as **single agent systemic treatment** combining PD-L1 targeted anti-CD47 effector delivery

Robust non-clinical activity demonstrating potential **wide therapeutic index**

LB101 first candidate from modular **LockBody platform**

LB101: Designed to optimally deliver PD-L1 targeted anti-CD47 activity to the TME

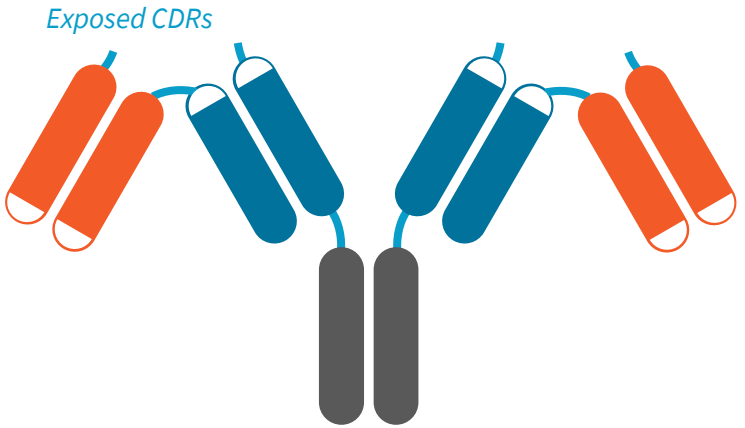
LOCKED



1. Constitutive Fabs drive tumor enrichment

2. Natural cleavage of IgG-derived hinges in tumors

UNLOCKED



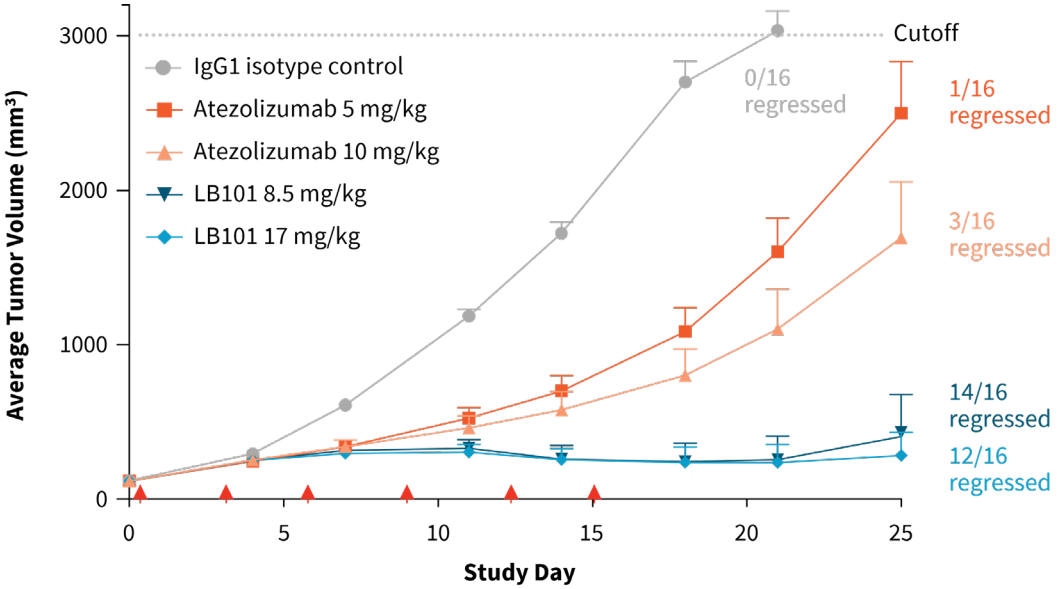
Peripheral Stability: IgG1 hinges naturally resistant to cleavage in serum

Tumor Unlocking: IgG1 hinges susceptible to cleavage in diseased tissue by various natural processes

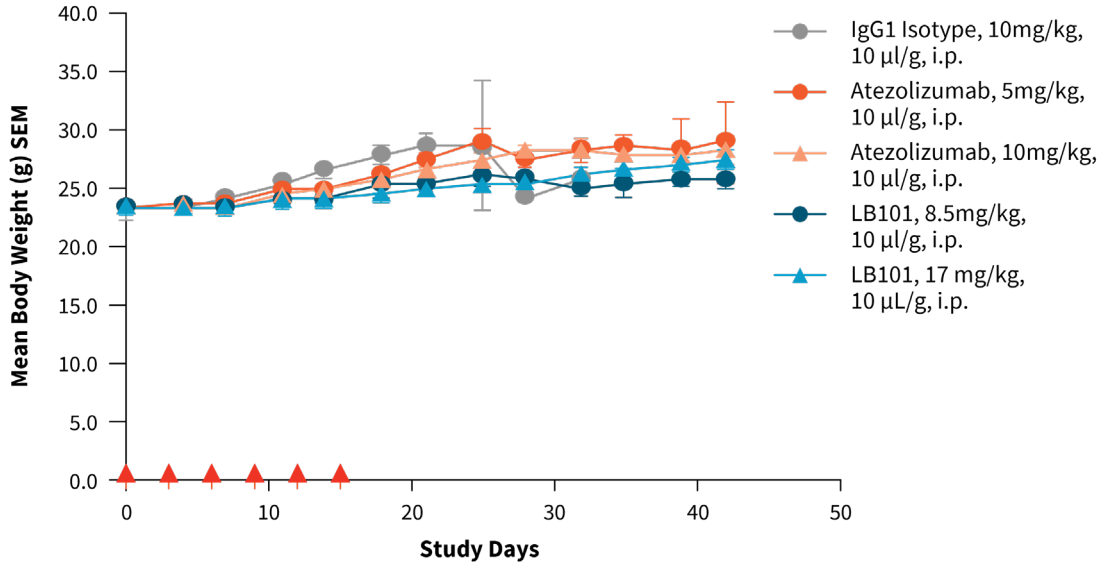
TME is tumor micro-environment

LB101 showed improved efficacy and durability over atezolizumab in a difficult-to-treat mouse model while being well tolerated

In vivo: Systemically delivered LB101 exhibited significant tumor regression



In vivo: LB101 was well tolerated with no weight loss



CENTESSA PHARMACEUTICALS

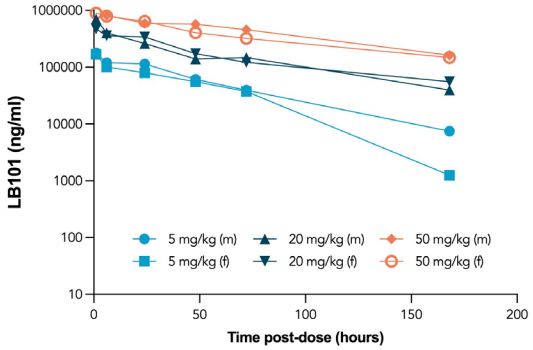
Note: MC38 hPD-L1+ syngeneic model in mouse; Arrows indicate dosing every 3 days (Q3d x 6) at Days 0, 3, 6, 9, 12, and 15. 5 mg/kg of atezolizumab is equivalent to 8.5 mg/kg of LB101.

LB101 shown to be safe and well tolerated in non-human primates up to 50 mg/kg weekly x 4 weeks

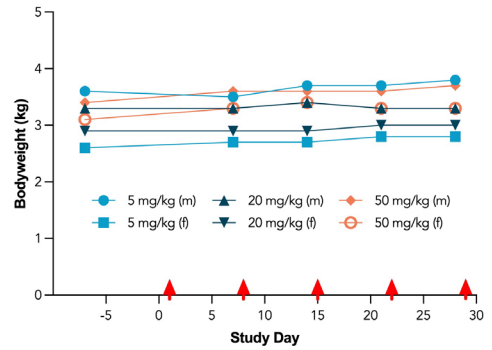
***In-vivo:* LB101 delivered IV at 5, 20, 50mg/kg (q7d x 4) in non-human primates**

- Human IgG1-like PK
- No adverse observations
  - No anemia or thrombocytopenia
  - No changes in pathology, clinical chemistry or coagulation parameters

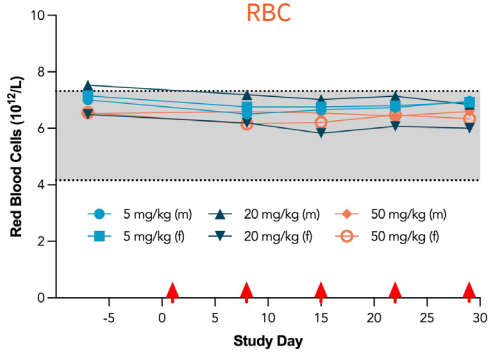
Pharmacokinetics



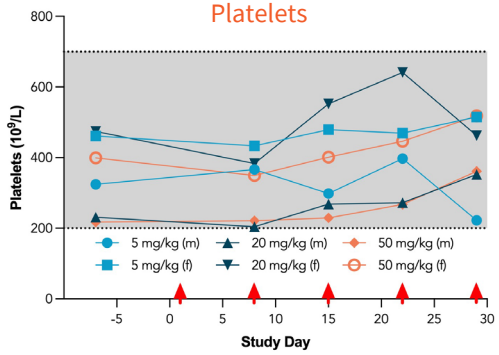
Bodyweight



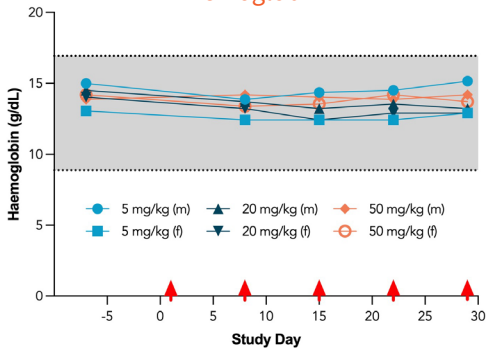
RBC



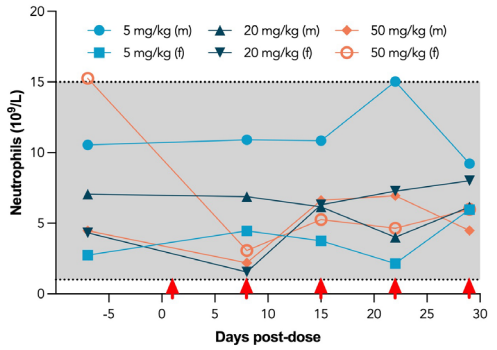
Platelets



Hemoglobin



Neutrophils



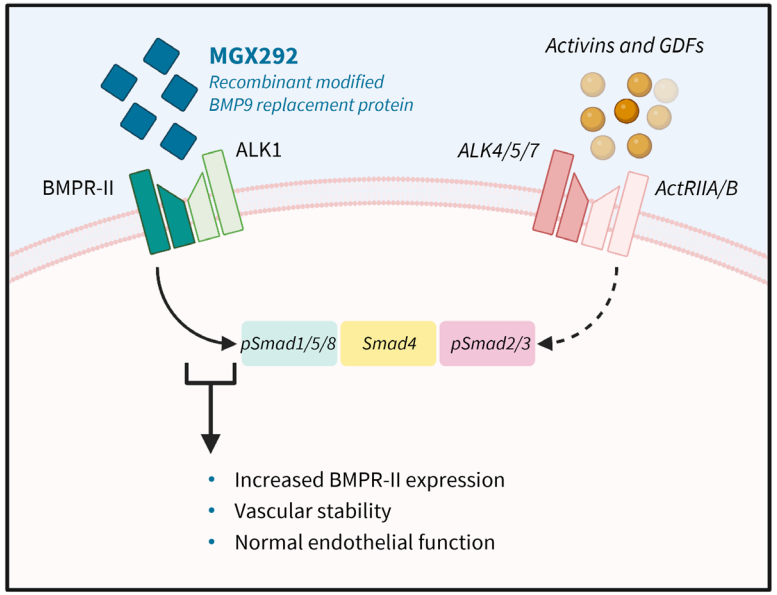
CENTESSA PHARMACEUTICALS

MGX292 in Pulmonary Arterial Hypertension

MGX292: Potential for disease modification in patients with PAH

Protein-engineered variant of BMP9, selective for BMPR2/ALK2

MGX292 Mechanism



- BMP9/BMPR2 axis is a **genetically validated target** for pulmonary arterial hypertension (PAH)
- MGX292 is designed to directly **impact the central pathway** that is deficient in PAH: endothelial BMP9 signaling

Novel MoA with potential for **disease modification**

Designed to directly **impact BMP9 signaling** genetically missing or deficient in PAH and avoid undesired bone formation

In vivo data observed **normalization of lung vascular pathology**

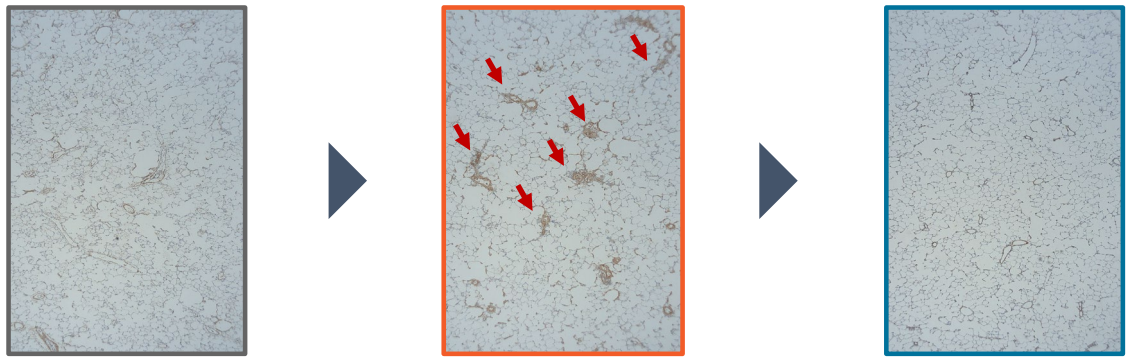
~ 70,000
Patients with PAH in North America, Europe and Japan

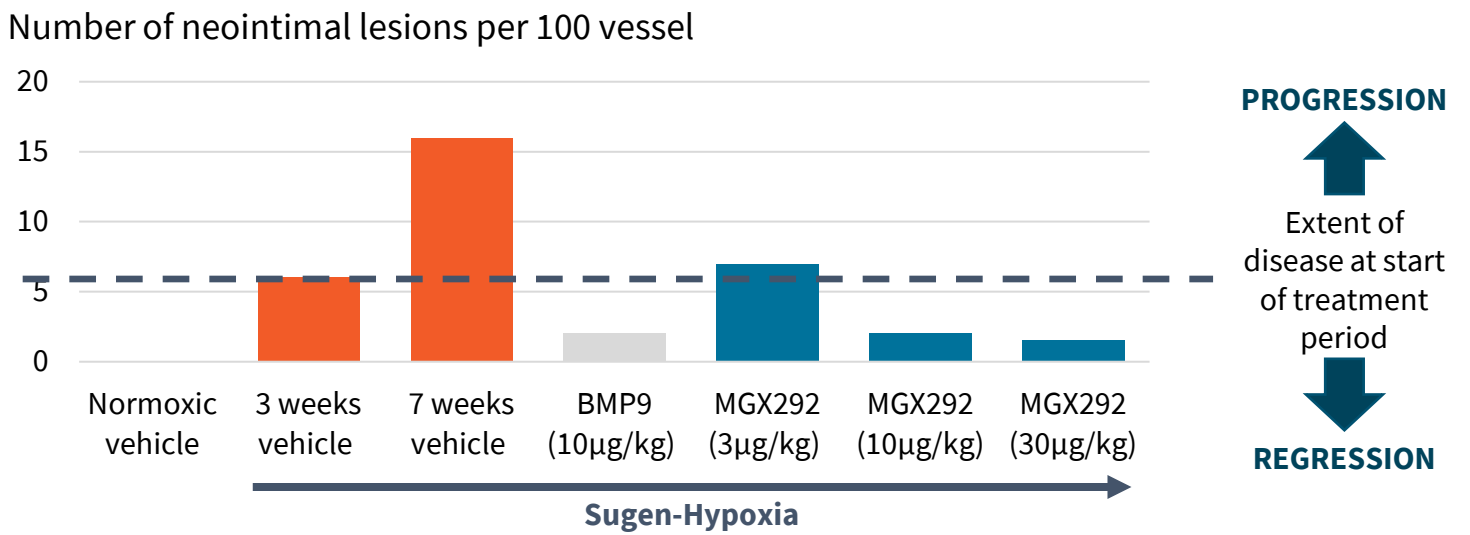
~$6B+
PAH Global Market [1]

*Source: 1. Evaluate Pharma 2021

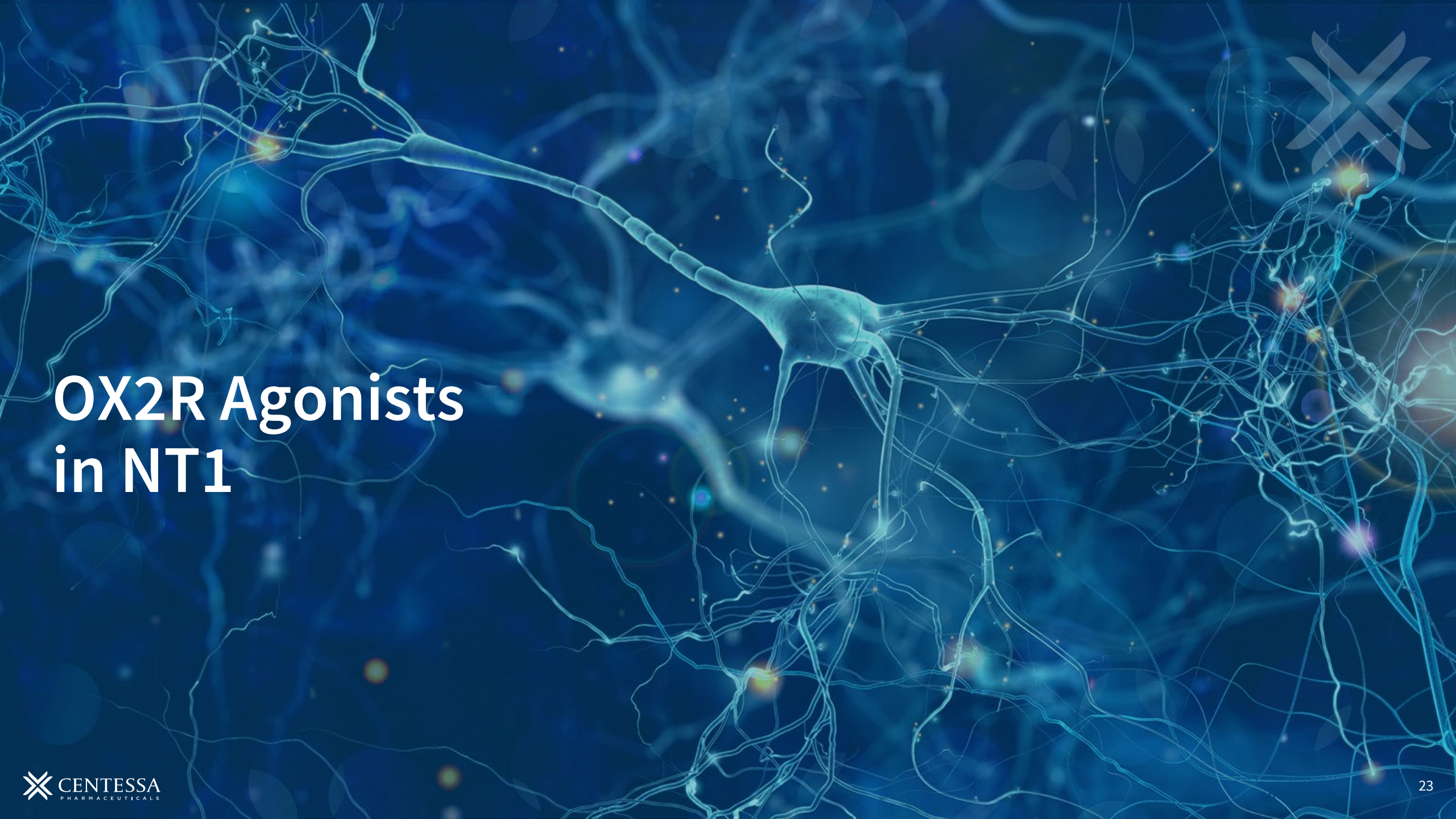
Preclinical Data: MGX292 demonstrated dose-dependent normalization of established lung vascular pathology in Sugen-hypoxia rat model

MGX292[1] shown to modify 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



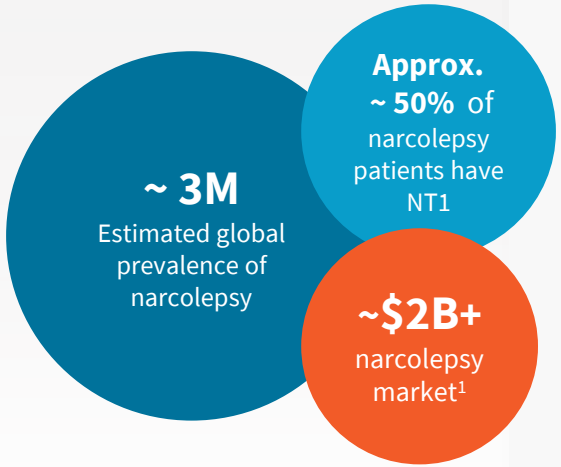
OX2R Agonists in NT1

OX2R Agonists: Potential to change the standard of care for narcolepsy

Narcolepsy Type 1 (NT1)

A rare neurological condition that affects the brain's ability to regulate the normal sleep-wake cycle

Caused by a profound loss of orexin neurons in the brain



High unmet need

Current treatments do not restore normal function, and NT1 symptoms persist despite polypharmacy

- **75%** patients experience EDS[1]
- **50%** patients still have 1-2 cataplexy episodes per day[2]

OX2R agonists designed to **reactivate orexin** signaling in the brain

Highly validated human target

Clinical proof of concept (PoC) for efficacy in NT1 and in other sleep/wake disorders[3]

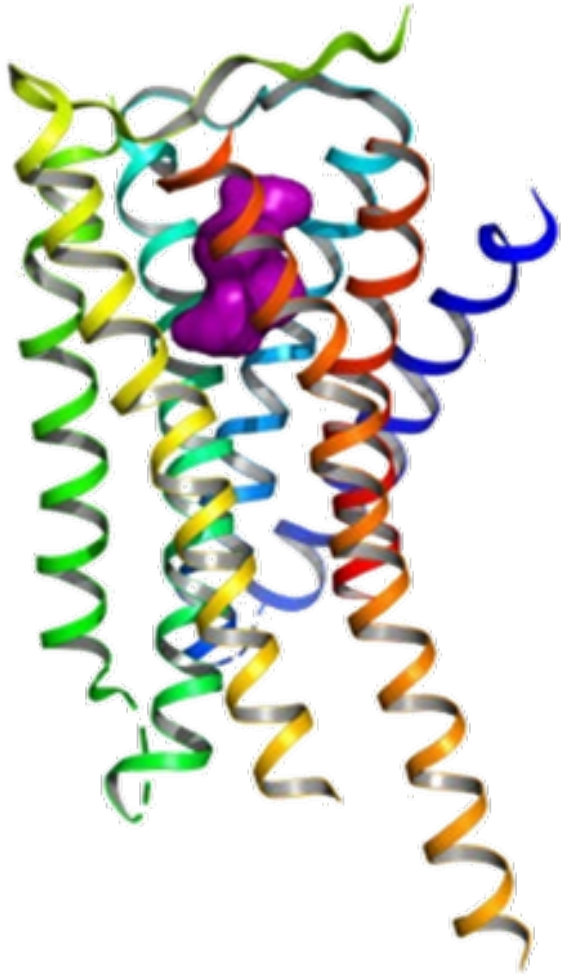
EDS is excessive daytime sleepiness.

1. Evaluate Pharma 2021. 2. Maski K, et al. J Clin Sleep Med 2017;13;419–25. 3. Evans, R, et al. PNAS 2022: 119; 35; e2207531119.

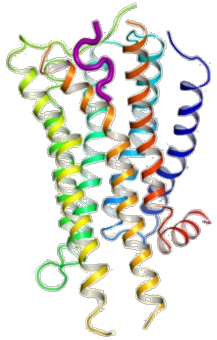
Structure-based drug design has enabled the discovery of OX2R agonists with potential as orexin signaling replacement therapy for NT1

Discovery compounds have demonstrated **sub-nanomolar potency** in *in vitro* assays *

* Based on EC50, *in vitro* functional profiles of exemplar small molecule agonists and exemplar peptide agonists in a calcium mobilization FLIPR assay with cells expressing recombinant human OX2R



Example X-ray structure of OX2R with small molecule orexin agonist (shown in purple)

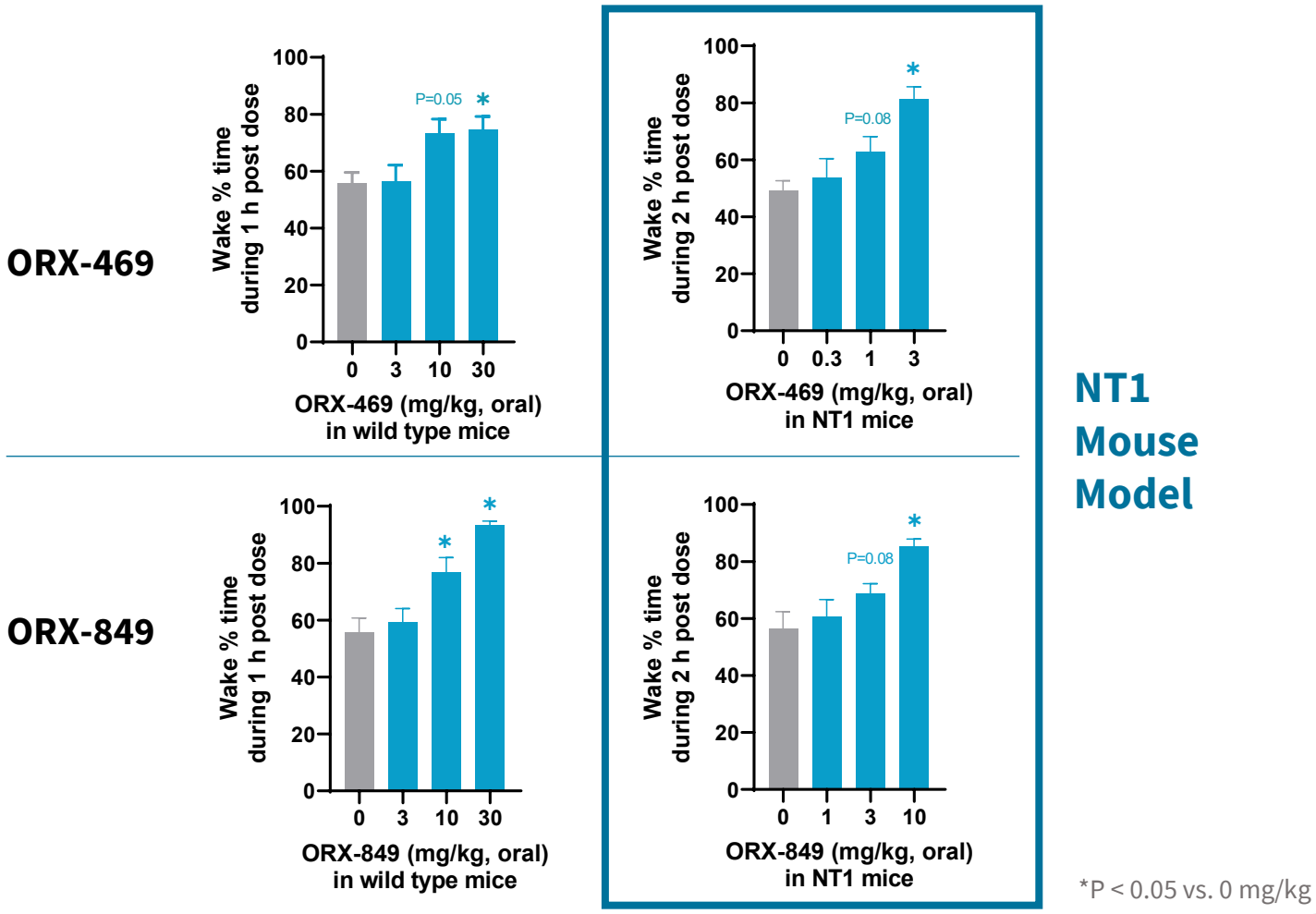


Example Cryo-EM structure of OX2R with peptide agonist (shown in purple)

CENTESSA PHARMACEUTICALS

Novel OX2R agonists increased wakefulness in WT and NT1 mice

Exemplar small molecule agonists



*P < 0.05 vs. 0 mg/kg

- Novel small-molecule OX2R agonists from multiple lead series increased wakefulness in healthy mice and in an NT1 mouse model.
- The newest compounds showed substantially increased potency in NT1 mice and are progressing rapidly through the discovery pipeline.

Poster Presentation entitled, "Novel Orexin Receptor-2 Agonists Developed Using Structure-based Drug Design: Prototype Compounds Promote Wakefulness and Reduce Cataplexy in Orexin/Ataxin-3 and WT Mice." Presented at 26th Conference of the European Sleep Research Society, Sept. 30, 2022. Note: Wakefulness detected by piezoelectric monitoring, which is a rapid, non-invasive method for classifying sleep and wakefulness by unsupervised machine learning.

Centessa is fueling multiple pathways to value creation

- Multiple potential blockbuster assets
- Cash runway into 2026 enables clinical readouts across pipeline
- World-class R&D team

Note: **$444.8 million** in cash and cash equivalents as of September 30, 2022.


CENTESSA
PHARMACEUTICALS