UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

Date of Report (date of earliest event reported): September 12, 2022

CENTESSA PHARMACEUTICALS PLC

(Exact name of Registrant, as specified in its charter)

England and Wales	**001-04321**	**98-1612294**
(State or other jurisdiction of incorporation)	(Commission File Number)	(I.R.S. Employer Identification Number)

Mailing address:
3rd Floor
1 Ashley Road
Altrincham
Cheshire WA14 2DT
United Kingdom
(Address of principal executive offices) (Zip code)

Registrant's telephone number, including area code: +**44 (0) 203 920 6789, ext. 9999**

Former name or address, if changed since last report:

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	**Trading Symbol(s)**	**Name of each exchange on which registered**
Ordinary shares, nominal value £0.002 per share	CNTA	Nasdaq Stock Market, LLC*
American Depositary Shares, each representing one ordinary share, nominal value £0.002 per share	CNTA	Nasdaq Stock Market, LLC

*Not for trading, but only in connection with the listing of the American Depositary Shares on The Nasdaq Stock Market, LLC.

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure.

The Company from time to time presents and/or distributes to the investment community at various industry and other conferences slide presentations to provide updates and summaries of its business. The Company is posting to the "Investors" portion of its website at www.centessa.com a copy of its current corporate slide presentation. These slides are attached to this Current Report on Form 8-K as Exhibit 99.1. The Company undertakes no obligation to update, supplement or amend the materials attached hereto as Exhibit 99.1.

The information in this Current Report on Form 8-K (including Exhibit 99.1) shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such a filing.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	
99.1	Corporate presentation prepared as of September 12, 2022

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Date: September 12, 2022

By:	/s/ Saurabh Saha
Name:	Saurabh Saha, M.D., Ph.D.
Title:	Chief Executive Officer


CENTESSA
PHARMACEUTICALS
Corporate
Overview
Asset-Centric. Patient-Centric.
September 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. 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 truly transformational for patients

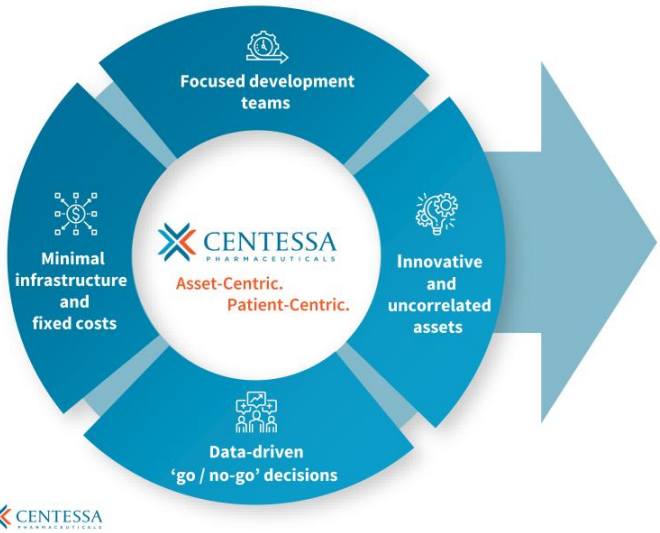
- Multiple potential blockbuster assets with clinical readouts anticipated over next two years
- Cash runway into 2026 enables clinical proof of concept readouts across portfolio
- World-class R&D team

CENTESSA PHARMACEUTICALS

Note: **$484.2 million** in cash and cash equivalents as of June 30, 2022.

DIFFERENTIATION

We are a transformational pharmaceutical company fueling an innovative pipeline



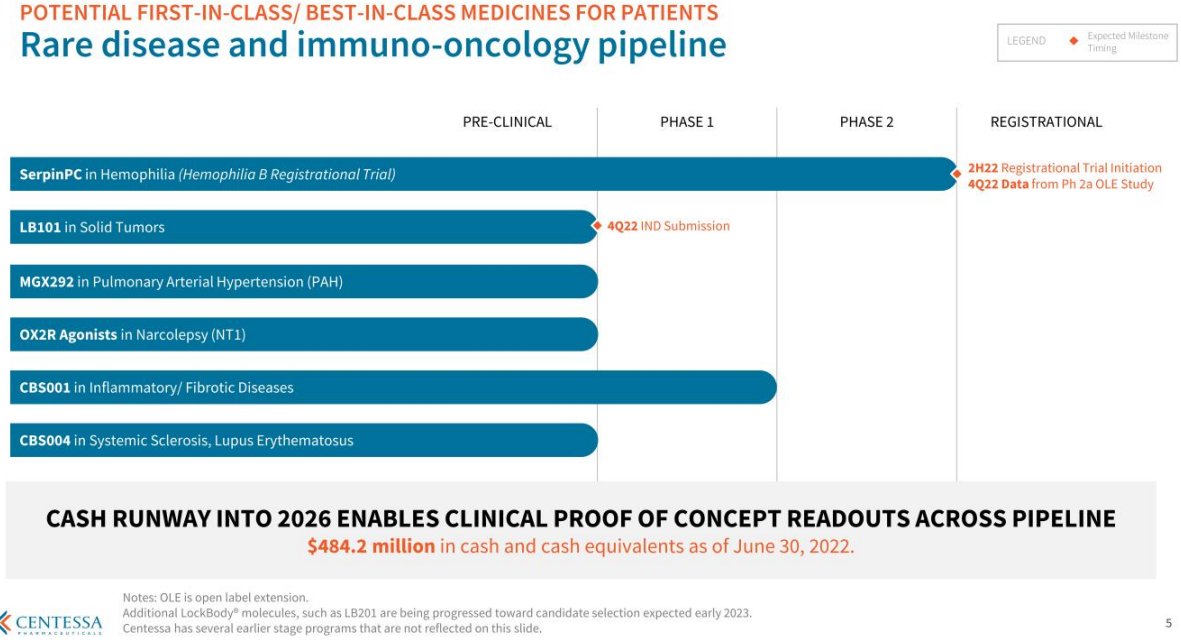
MULTIPLE PATHWAYS TO SIGNIFICANT VALUE CREATION

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 [2]internal estimates
Centessa has several earlier stage programs that are not reflected on this slide.

POTENTIAL FIRST-IN-CLASS/ BEST-IN-CLASS MEDICINES FOR PATIENTS

Rare disease and immuno-oncology pipeline



CASH RUNWAY INTO 2026 ENABLES CLINICAL PROOF OF CONCEPT READOUTS ACROSS PIPELINE

$484.2 million in cash and cash equivalents as of June 30, 2022.

Notes: OLE is open label extension.
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 focused on execution

SAURABH SAHA MD PhD
Chief Executive Officer
Bristol Myers Squibb · NOVARTIS · Deltina · ATLAS VENTURE · McKinsey&Company

ANTOINE YVER MD MSc
EVP & Chairman of Development
Johnson&Johnson · AstraZeneca · Schering-Plough · MERCK · RHÔNE-POULENC · Aventis

DAVID GRAINGER PhD
Chief Innovation Officer
medicxi · RxCelerate · totalscientific · Index Ventures

JAVAD SHAHIDI MD MSc
Chief Medical Officer
Lilly · BAYER

GREG WEINHOFF MD MBA
Chief Financial Officer
ARVELLE · CHL HEALTHCARE PARTNERS · Morgan Stanley · Amicus · AXOVANT

TIA BUSH
Chief Quality Officer
AMGEN

DAVID CHAO PhD
Chief Administrative Officer
BIOMED VALLEY · McKinsey&Company · NOVARTIS

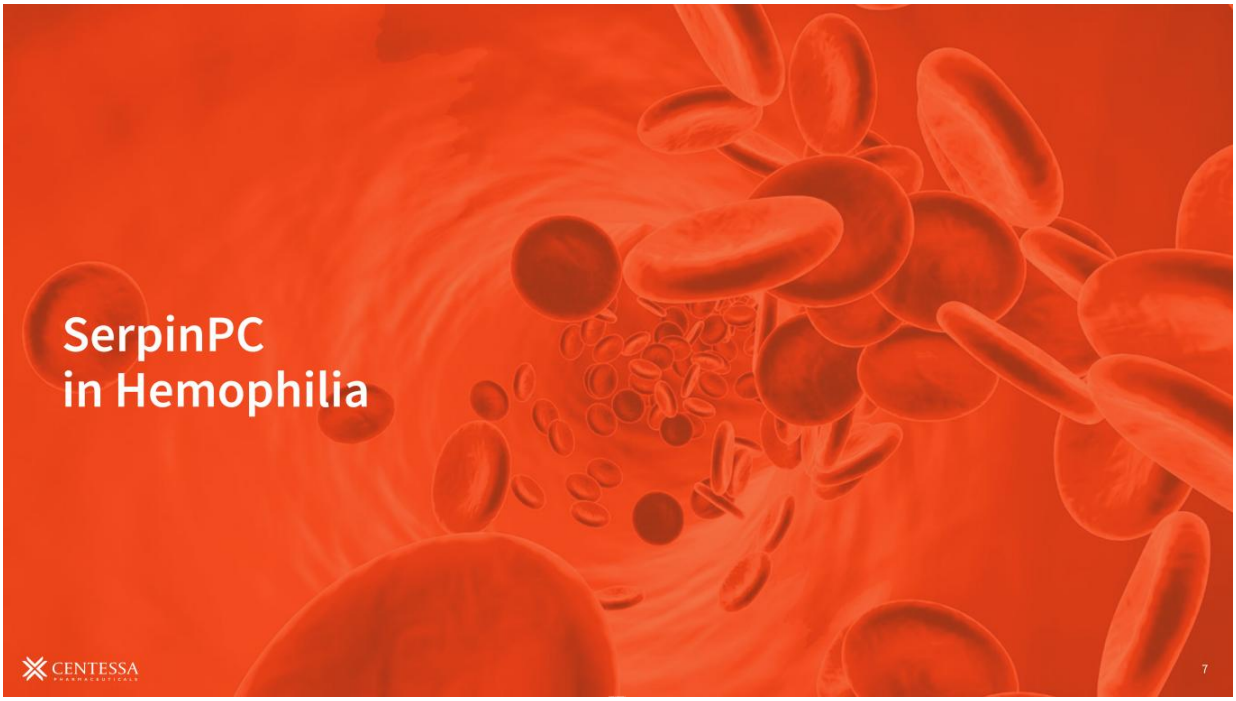
THOMAS TEMPLEMAN PhD
Chief Technology Officer
AXOVANT · Hospira · graybug · MEDIVATION · Johnson&Johnson · LIQUIDIA

IQBAL HUSSAIN
General Counsel
ReedSmith · SLAUGHTER AND MAY · ROPES&GRAY · Johnson&Johnson

JOSH HAMERMESH MBA
SVP, Business Development
gamida cell · LOCUST WALK · Infinity · molecularinsight pharmaceuticals · Pervasis · genzyme

KRISTEN SHEPPARD ESQ.
SVP, Investor Relations & Corp. Comm.
Dicerna · STAGE · Akebia · EQUALLOGIC · enfavasys

CENTESSA PHARMACEUTICALS


SerpinPC
in Hemophilia
CENTESSA
PHARMACEUTICALS
7

SerpinPC: Potential transformative therapy in hemophilia

Inhibitor of APC designed to prevent and reduce bleeds without risk of thrombosis; initial focus hemophilia B

SerpinPC

SIGNIFICANT OPPORTUNITY TO ADDRESS GLOBAL HEMOPHILIA POPULATION

Current hemophilia B treatments require IV infusions

Pipeline agents carry potential risk of thrombosis

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

Novel MoA; **Non-factor** approach

Significant **reduction in bleeding[2]**

Potential **best-in-class safety profile:** No thrombosis observed[2]

Convenient **subcutaneous** dosing

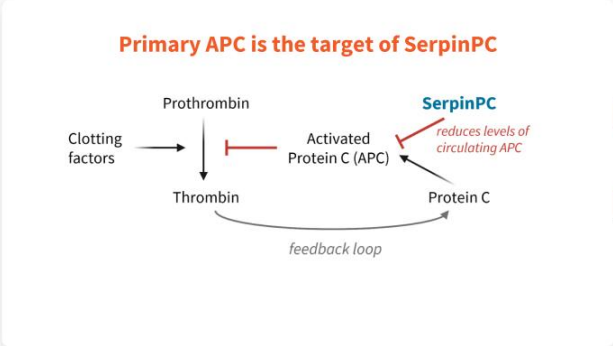
STATUS:

Phase 2a open label extension (OLE) data expected Q422

Registrational studies for hemophilia B expected to start 2H22

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. 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.

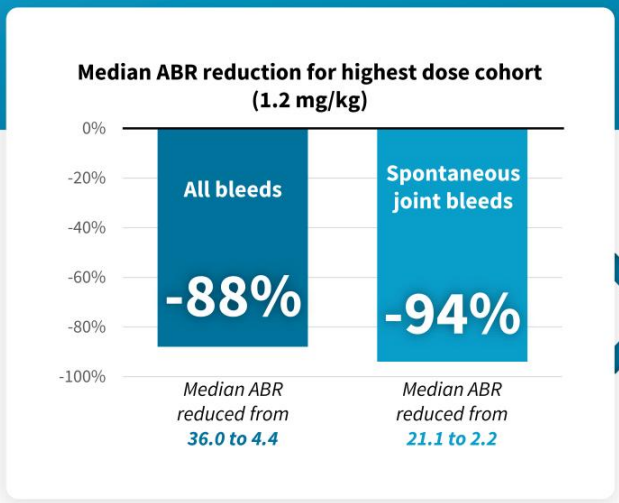
SerpinPC is believed to have a unique MoA supported by human genetics



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

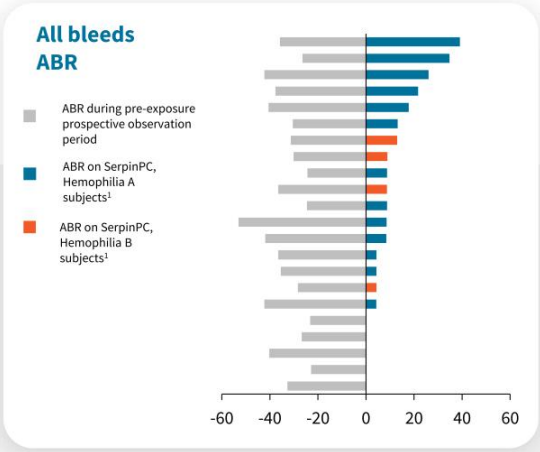
Across all dose levels:

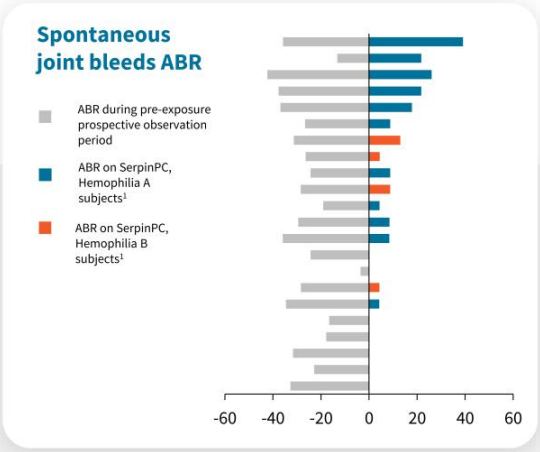
- No thrombosis
- No instances of sustained elevations in D-dimer

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

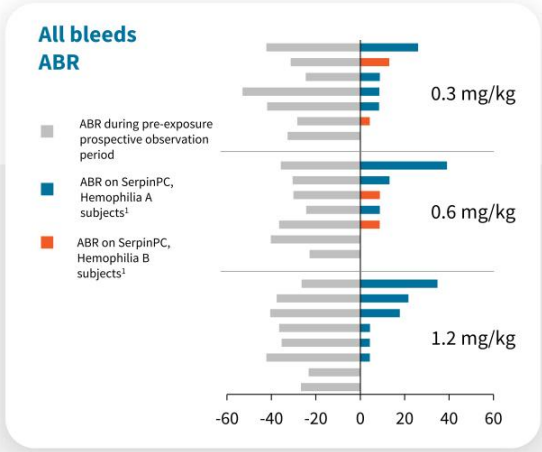
Phase 2a Study: Individual observed ABRs for all bleeds and spontaneous joint bleeds

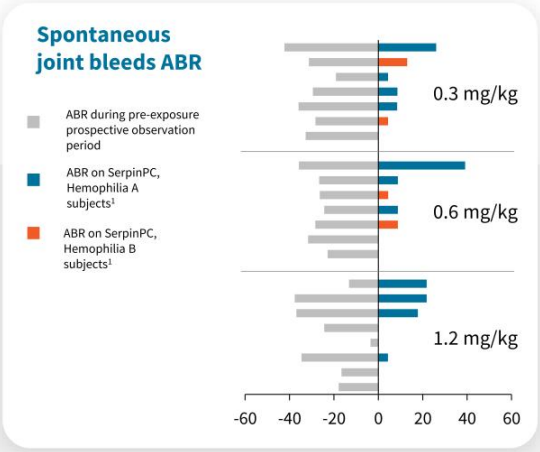




Six-month update of Phase 2a Study. ABR is annualized bleeding rate. 1. During second 12 weeks of exposure (as prespecified in the statistical analysis plan). Once monthly injections.

Phase 2a Study: Individual observed ABRs across dose cohorts



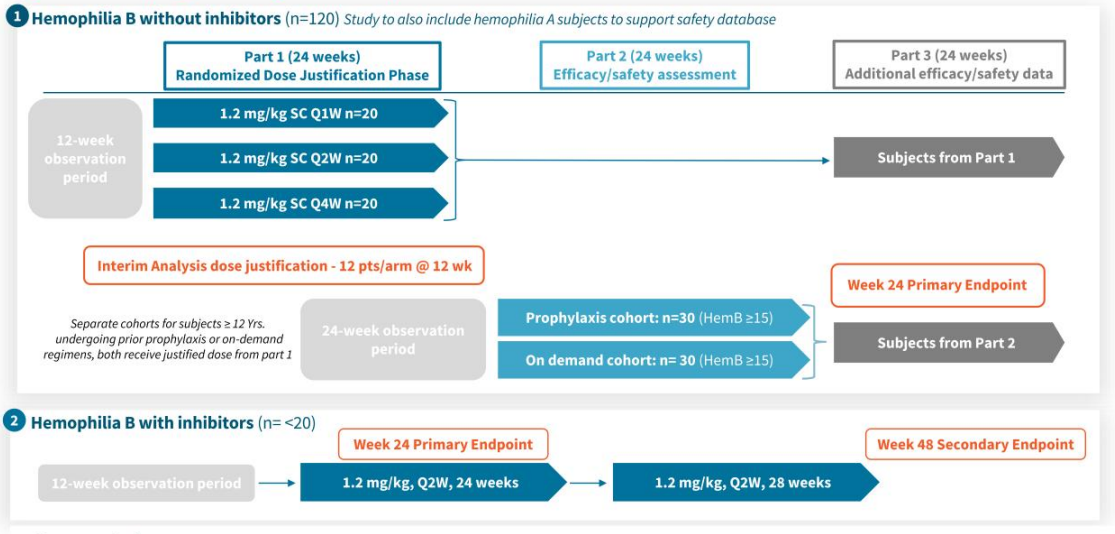


CENTESSA PHARMACEUTICALS

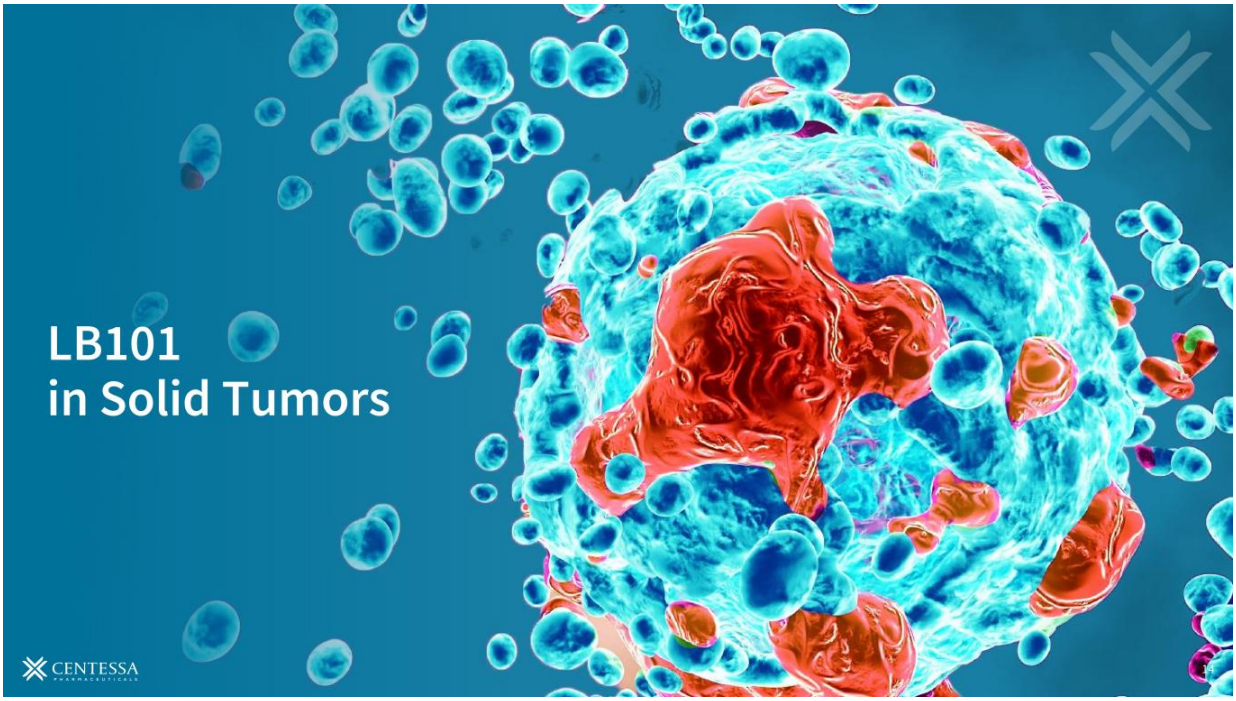
Six-month update of Phase 2a Study. ABR is annualized bleeding rate. 1. During second 12 weeks of exposure (as prespecified in the statistical analysis plan). Once monthly injections.

SerpinPC registrational studies expected to start 2H 2022

Registrational program design for hemophilia B



Primary Endpoint: Rate of treated bleeds (expressed as annualized bleeding rate [ABR]) in the observation period and during the first 24 weeks with SerpinPC

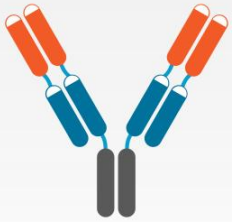

LB101
in Solid Tumors
CENTESSA

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

Pioneering our novel LockBody® pharmacology

LockBody

"It's all about the hinge"



Novel pharmacology focused on **human IgG-derived hinges** susceptible to natural hinge clipping

Designed as **single agent systemic treatment** combining PD-L1xCD-47

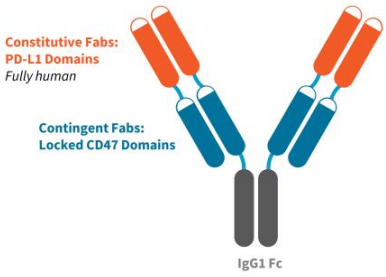
Robust preclinical activity demonstrating potential **wide therapeutic index**

LB101 first candidate from modular **LockBody platform**

STATUS: **IND submission planned for late 2022; Additional LockBody candidates expected in 2023**

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

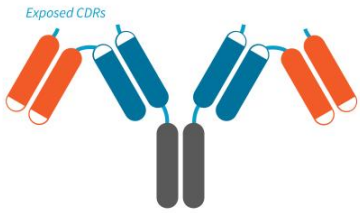
LOCKED



Peripheral Stability: IgG1 hinges naturally resistant to cleavage in serum

Constitutive Fabs drive tumor enrichment
+
Natural cleavage of IgG-derived hinges in tumors

UNLOCKED

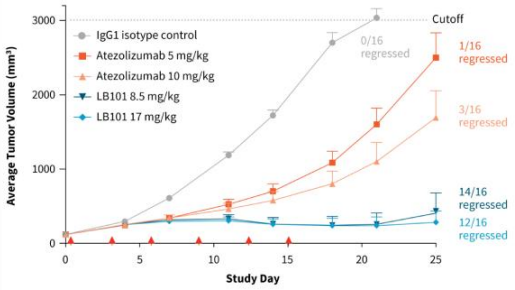


Tumor Unlocking: IgG1 hinges susceptible to cleavage in diseased tissue by various natural processes

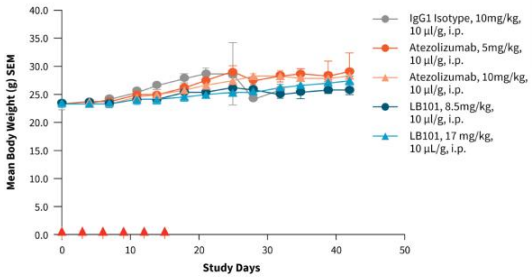
TME is tumor micro-environment

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

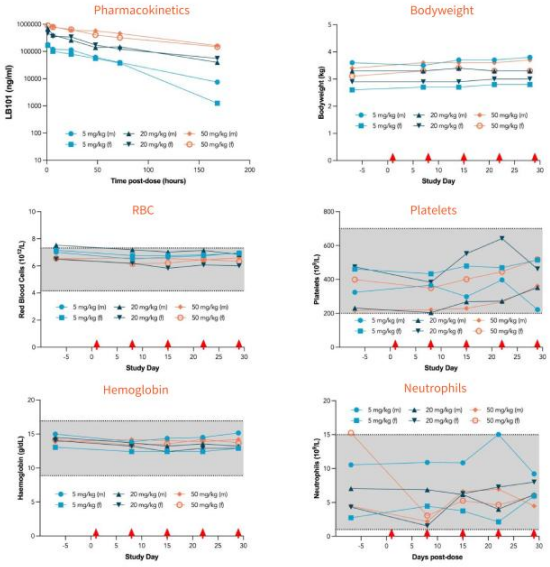


Note: MC38 hPD-L1+ syngeneic model in mouse; Arrows indicate dosing every 3 days (Q3d x 6) at Days 0, 3, 6, 9, 12, and 15. 5 mg/kg of atezolizumab is equivalent to 8.5 mg/kg of LB101.

LB101 shown to be safe and well tolerated in non-human primates

***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 impact on any hematology (no anemia or thrombocytopenia)
  - No changes in pathology, clinical chemistry or coagulation parameters

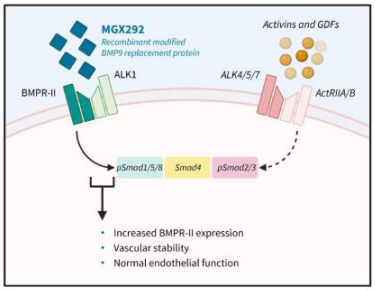



MGX292 in
Pulmonary
Arterial
Hypertension
CENTESSA
19

MGX292: Potential for disease reversal 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 specifically **activates the central pathway** that is deficient in PAH: endothelial BMP9 signaling

Novel MoA with potential for **disease reversal**

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

In vivo data demonstrated **reversal of lung vascular pathology**

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

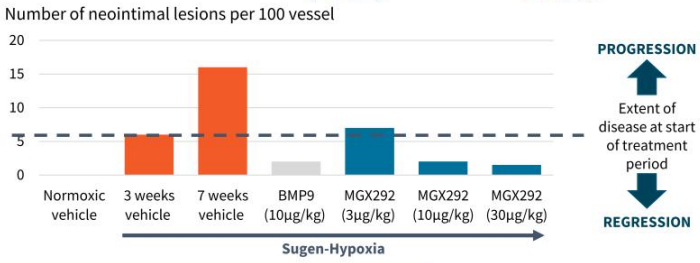
~$6B+
PAH Global Market [1]

CENTESSA PHARMACEUTICALS

*Source: 1. Evaluate Pharma 2021

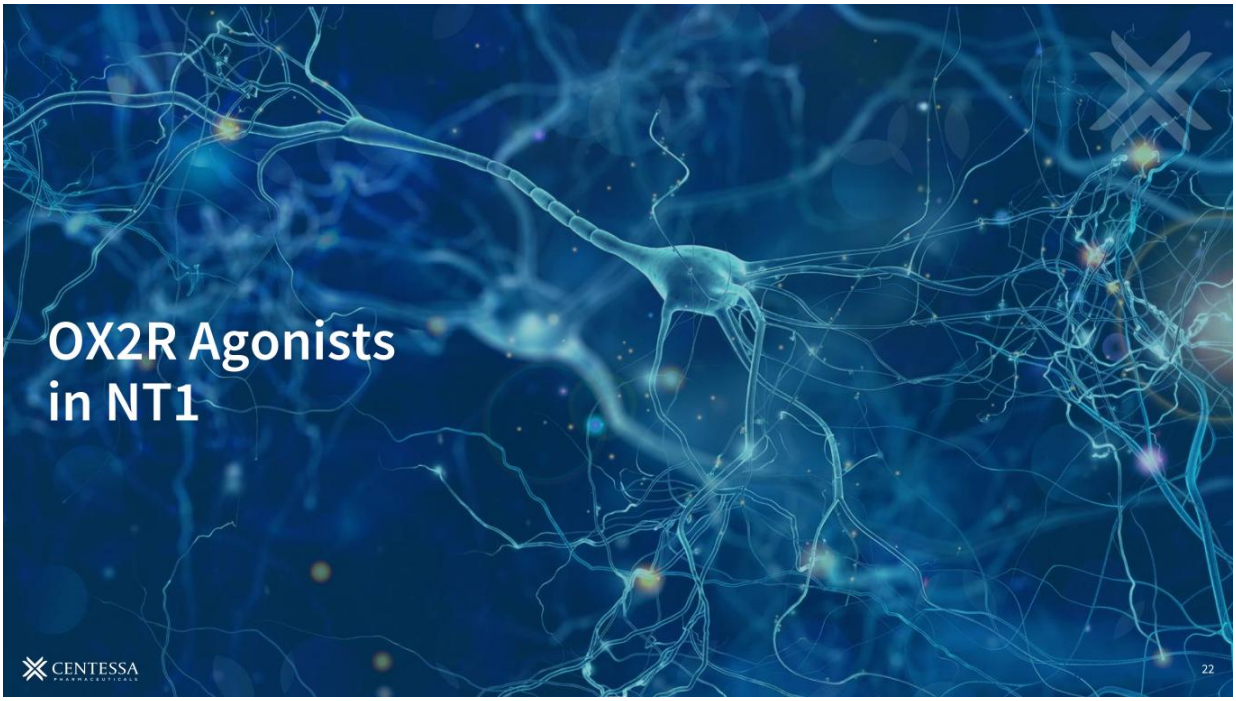
Preclinical Data: MGX292 demonstrated dose-dependent reversal of established lung vascular pathology in Sugen-hypoxia rat model

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



CENTESSA PHARMACEUTICALS

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

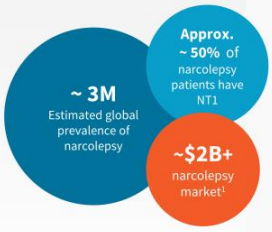

OX2R Agonists
in NT1
CENTESSA
PHARMACEUTICALS
22

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 genet**ic target

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

CENTESSA PHARMACEUTICALS

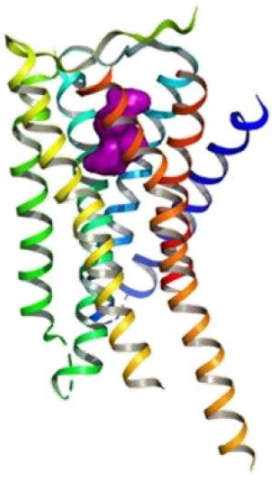
EDS is excessive daytime sleepiness.

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.

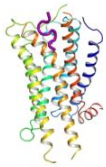
Structure-based drug design has enabled the discovery of OX2R agonists with potential as replacement therapy for NT1

The newest 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)

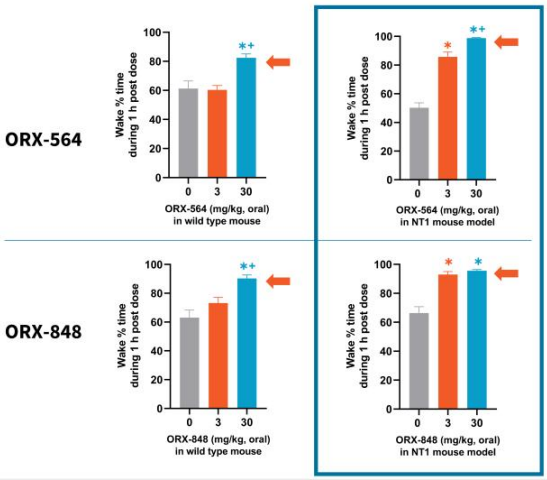


Example Cryo-EM structure of OX2R with peptide agonist (shown in purple)

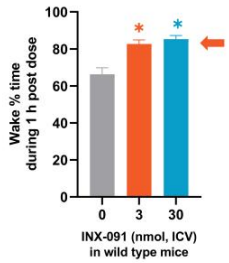
CENTESSA PHARMACEUTICALS

Novel OX2R agonists increase wakefulness in WT and NT1 mice

Exemplar small molecule agonists



Exemplar peptide agonist



ICV is intracerebroventricular administration

For all graphs: *P < 0.05 vs. 0 mg/kg; +P < 0.05 vs. 3 mg/kg

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 with clinical readouts anticipated over next two years
- Cash runway into 2026 enables clinical proof of concept readouts across portfolio
- World-class R&D team

Note: **$484.2 million** in cash and cash equivalents as of June 30, 2022.


CENTESSA
PHARMACEUTICALS
27