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): March 30, 2023

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 2.02 Results of Operations and Financial Condition.

On March 30, 2023, Centessa Pharmaceuticals plc (the "Company") announced its financial results for the quarter ended December 31, 2022. The full text of the press release issued in connection with the announcement is furnished as Exhibit 99.1 to this Current Report on Form 8-K.

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 a copy of its current corporate slide presentation to the "Investors" portion of its website at www.centessa.com/events-presentations. These slides are attached to this Current Report on Form 8-K as Exhibit 99.2. The Company undertakes no obligation to update, supplement or amend the materials attached hereto as Exhibit 99.2.

The information in this Current Report on Form 8-K (including Exhibits 99.1 and 99.2) 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	Press Release dated March 30, 2023
99.2	Corporate Presentation prepared as of March 30, 2023
104	Cover Page Interactive Data (embedded within the Inline XBRL document)

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: March 30, 2023

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

Exhibit 99.1

Centessa Pharmaceuticals Reports Recent Business Progress and Financial Results for the Fourth Quarter and Full-Year 2022

– Initiated registration program for SerpinPC to treat hemophilia B; Enrolling subjects in PRESent-5, observational study –

– First subject dosed in Phase 1/2a clinical trial for LB101, a PD-L1xCD47 LockBody® to treat solid tumors; Preclinical data from second LockBody program targeting PD-L1xCD3 expected in 2023 –

– Nominated ORX750, an orally administered, selective orexin receptor-2 (OX2R) agonist, as product candidate with the potential to be a best-in-class therapy to treat narcolepsy and other sleep disorders; ORX750 profile to be presented at scientific meeting in 2023 –

– Cash runway into 2026 –

BOSTON and LONDON, March 30, 2023: Centessa Pharmaceuticals plc (Nasdaq: CNTA), a clinical-stage pharmaceutical company focused on discovering and developing medicines that are transformational for patients, today reported recent business progress and financial results for the fourth quarter and full-year ended December 31, 2022.

“Centessa made substantial progress in 2022, highlighted by the achievement of important milestones toward our goal of bringing transformational medicines to patients," said Saurabh Saha MD PhD, Chief Executive Officer of Centessa. “We advanced key clinical and development objectives, prioritized our pipeline, and continued to manage our resources with timely data and science-driven decisions, consistent with our asset-centric model. As a result, we entered 2023 with solid momentum on our pipeline programs that we believe have the greatest potential to transform the lives of patients with unmet medical needs."

Dr. Saha continued, “Our most advanced product candidate is SerpinPC, a subcutaneously administered novel inhibitor of activated protein C (APC), which is in a registrational program for the treatment of hemophilia B. In December 2022, we presented data from a Phase 2a study showing SerpinPC to have a favorable safety and tolerability profile, as well as evidence of sustained efficacy in patients with hemophilia as measured by a reduction in the all-bleeds annualized bleeding rates (ABR). We believe these data support the potential for SerpinPC to be a first-in-class subcutaneously administered therapy with a differentiated safety profile for individuals with hemophilia, subject to regulatory review and approval. We are excited to be enrolling subjects in PRESent-5, an observational feeder study, and are preparing to begin dosing in the PRESent-2 and PRESent-3 interventional studies this year."

"We are also very pleased to announce the dosing of the first subject in the Phase 1/2a clinical trial of LB101, a conditionally tetravalent PD-L1xCD47 bispecific monoclonal antibody from our LockBody technology platform for the treatment of solid tumors. LB101 is the first LockBody candidate we have brought to the clinic, and we look to this study to provide valuable insights regarding the safety and tolerability profile of LB101, as well as the performance of our LockBody platform in a clinical setting. Following LB101 is our second LockBody program targeting PD-L1xCD3, for which we expect to name a product candidate this year," said Dr. Saha.

“Lastly, our team is excited to be advancing ORX750, an orally administered, selective orexin receptor-2 (OX2R) agonist, as our product candidate for the treatment of narcolepsy with potential expansion into other sleep disorders. We believe ORX750 has the potential to be a best-in-class therapy for the treatment of narcolepsy and look forward to sharing the candidate profile at a scientific meeting later this year," said Dr. Saha.

Dr. Saha concluded, “We are thrilled with the momentum at Centessa and believe we are well positioned with a cash runway into 2026 to support the potential for multiple clinical readouts across our pipeline.”

Recent Highlights

- In January 2023, the Company announced clearance of its Investigational New Drug (IND) application from the U.S. Food and Drug Administration (FDA) to initiate a Phase 1/2a first-in-human clinical trial of LB101 for the treatment of solid tumors. The first subject was dosed in March 2023.
- In December 2022 and February 2023, the Company presented data from the open-label extension (OLE) of the ongoing Phase 2a study of SerpinPC for the treatment of hemophilia during oral presentations at the American Society of Hematology (ASH) Annual Meeting and the 16th Annual Congress of the European Association for Haemophilia and Allied Disorders (EAHAD), respectively. With total exposure of over 40 patient-years across multiple dosing regimens, the Phase 2a data showed a continued favorable safety and tolerability profile for SerpinPC, as well as evidence of sustained efficacy, as measured by a reduction in the all-bleeds ABRs. There were no thromboembolic events and no treatment-related sustained elevations of D-dimer observed across the Phase 2a study, to date. D-dimer is a sensitive measure of excessive thrombin generation.
- In December 2022, the Company began enrolling subjects into PRESent-5, an observational study in the SerpinPC registrational program for the treatment of hemophilia B.

Anticipated Upcoming Program Milestones

- **Hemophilia (SerpinPC)-** The registrational program for hemophilia B is ongoing. PRESent-5, an observational study, is enrolling subjects and the Company expects to begin dosing in PRESent-2 and PRESent-3 later this year. In addition, the Company expects to share data from Part 5 of the OLE of the Phase 2a study of SerpinPC, subject to completion, at a scientific meeting this year.
- **Solid Tumors**
  - **PD-L1xCD47 LockBody (LB101)-** The Phase 1/2a first-in-human clinical study is ongoing.
  - **PD-L1xCD3 LockBody (Undisclosed)-** The Company expects to name a product candidate and share preclinical data this year.
- **Narcolepsy and Other Sleep Disorders (ORX750)-** ORX750 was named as a product candidate and is currently in preclinical development and undergoing IND-enabling activities. The Company expects to share preclinical data at a scientific meeting later this year.

The Company expects to provide further updates on preclinical programs, including MGX292, as they advance towards clinical studies.

Fourth Quarter and Full-Year 2022 Financial Results

- **Cash and Cash Equivalents:** $393.6 million as of December 31, 2022, which the Company expects will fund operations into 2026, without drawing on the remaining available tranches under the Oberland credit facility.
- **Research & Development Expenses:** $27.8 million for the fourth quarter ended December 31, 2022, compared to $41.5 million for the fourth quarter ended December 31, 2021, and $155.1 million for the full-year 2022 compared to $95.7 million for the period from January 30, 2021 through December 31, 2021.
- **General & Administrative Expenses**: $13.8 million for the fourth quarter ended December 31, 2022, compared to $13.0 million the fourth quarter ended December 31, 2021, and $55.2 million for the full-year 2022 compared to $42.9 million for the period from January 30, 2021 through December 31, 2021.
- **Net Loss Attributable to Ordinary Shareholders:** $43.2 million for the fourth quarter ended December 31, 2022, compared to $60.8 million for the fourth quarter ended December 31, 2021, and $216.2 million for the full-year 2022 compared to $381.1 million for the period from January 30, 2021 through December 31, 2021.

About Centessa Pharmaceuticals

Centessa Pharmaceuticals plc is a clinical-stage pharmaceutical company that aims to discover and develop medicines that are transformational for patients. Our programs span discovery-stage to late-stage development and cover a range of high-value indications. We operate with the conviction that each one of our programs has the potential to change the current treatment paradigm and establish a new standard of care. For more information, visit http://www.centessa.com/, which does not form part of this release.

About SerpinPC

SerpinPC is a subcutaneously administered novel inhibitor of APC being developed as a potential treatment for hemophilia, regardless of severity or inhibitor status, and which may also be developed to prevent bleeding associated with other bleeding disorders. Centessa is advancing the registrational program for SerpinPC in hemophilia B, which includes a set of clinical studies with multiple components. PRESent-5, initiated in late 2022, is an observational feeder study to collect prospective observational data for minimum defined periods before switching to dosing subjects in the interventional studies. The interventional studies include PRESent-2 (moderately severe to severe hemophilia B without inhibitors, and severe hemophilia A with and without inhibitors) and PRESent-3 (hemophilia B with inhibitors). Additional information on the trials can be accessed at www.clinicaltrials.gov (NCT05605678, NCT05789524, NCT05789537). SerpinPC is an investigational agent that has not been approved by the FDA or any other regulatory authority.

About the LockBody Technology Platform and LB101

Centessa's proprietary LockBody technology platform aims to redefine immuno-oncology treatment for patients with cancer. LockBody drug candidates are designed to selectively drive potent effector function activity, such as CD47 or CD3, to the tumor micro-environment (TME) while avoiding systemic toxicity. The first LockBody candidate is LB101, a conditionally tetravalent PD-L1xCD47 bispecific monoclonal antibody which has two anti-CD47 domains blocked by two anti-PD-L1 domains, with proprietary human IgG-derived hinges linking the anti-CD47 and anti-PD-L1 domains. The cell-killing mechanism of action, CD47, is designed to be blocked by the PD-L1 tumor targeting domain until the IgG-derived hinges are naturally degraded in the TME, thus unlocking and activating the CD47 effector function activity in the tumor. LB101 is in a Phase 1/2a clinical trial. LB101 is an investigational agent that has not been approved by the FDA or any other regulatory authority.

Forward Looking Statements

This press release contains forward-looking statements. These statements may be identified by 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 that are intended to identify forward-looking statements. Any such statements in this press release that are not statements of historical fact may be deemed to be forward-looking statements, including statements related to the Company’s ability to discover and develop transformational medicines for patients; its expectations on executing the Company's pipeline; its expectations on its cash runway into 2026, which are based on certain assumptions; the timing of commencement of new studies or clinical trials or clinical and preclinical data related to SerpinPC, LB101, the LockBody technology platform, ORX750, MGX292 and other LockBody candidates; its ability to identify, screen and recruit a sufficient number of or any subjects in its anticipated new studies or clinical trials including PRESent-5, the observational feeder study, PRESent-2 and PRESent-3 and studies or trials of LB101 and any other LockBody candidates, its expectations on executing its research and clinical development plans and the timing thereof; the Company’s ability to differentiate SerpinPC, LB101, ORX750, MGX292 and other LockBody candidates from other treatment options; the development and therapeutic potential of SerpinPC, LB101, the LockBody technology platform, ORX750, MGX292, and other LockBody candidates; and regulatory matters, including the timing and likelihood of success of obtaining authorizations to initiate or continue clinical trials. Any forward-looking statements in this press release are based on our current expectations, estimates, assumptions and projections only as of the date of this release and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements. These risks and uncertainties include, but are not limited to, risks related to the safety and tolerability profile of our product candidates; our ability to identify, screen and recruit a sufficient number of or any subjects in our anticipated new studies or clinical trials including PRESent-2, PRESent-3, PRESent-5, and studies or trials of LB101 or within anticipated timelines; our ability to execute IND-enabling activities in a timely manner or at all, including with respect to ORX750; our ability to protect and maintain our intellectual property position; business (including commercial viability), regulatory, economic and competitive risks, uncertainties, contingencies and assumptions about the Company; risks inherent in developing product candidates 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/or commercialized; the risk that the results of preclinical studies or clinical studies will not be predictive of future results in connection with future studies; economic risks to the United States and United Kingdom banking systems; geo-political risks such as the Russia-Ukraine war and risks related to the COVID-19 pandemic including the effects of the Delta, Omicron and any other variants. These and other risks concerning our programs and operations are described in additional detail in our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, and our other reports, which are on file with the U.S. Securities and Exchange Commission (SEC). We explicitly disclaim any obligation to update any forward-looking statements except to the extent required by law.

Contact:
Kristen K. Sheppard, Esq.
SVP of Investor Relations
investors@centessa.com

Centessa Pharmaceuticals plc (Successor) and Centessa Predecessor Group (Predecessor)

Consolidated and Combined Statements of Operations and Comprehensive Loss

(unaudited)

(amounts in thousands except share and per share data)

	Successor				Predecessor
	Three Months Ended December 31, 2022	Three Months Ended December 31, 2021	Twelve Months Ended December 31, 2022	Period from January 30, 2021 through December 31, 2021	Period from January 1, 2021 through January 29, 2021
Operating expenses:					
Research and development	27,835	41,534	155,083	$ 95,660	$ 662
General and administrative	13,768	12,988	55,200	42,888	121
Change in fair value of contingent value rights	—	3,770	1,980	15,082	—
Acquired in-process research and development	—	—	—	220,454	—
Loss from operations	(41,603)	(58,292)	(212,263)	(374,084)	(783)
Interest (expense) income, net	(2,164)	(1,272)	(7,033)	(1,172)	(9)
Amortization of debt discount	—	—	—	—	(37)
Debt issuance costs	—	(1,331)		(1,331)	
Other income (expense), net	(70)	235	2,342	(4,370)	—
Loss before income taxes	(43,837)	(60,660)	(216,954)	(380,957)	(829)
Income taxes (benefit) expense	(664)	114	(747)	114	—
Net loss	(43,173)	(60,774)	(216,207)	(381,071)	(829)
Other comprehensive loss:					
Foreign currency translation adjustment	198	(2,050)	(2,185)	778	107
Total comprehensive loss	$ (42,975)	$ (62,824)	$ (218,392)	$ (380,293)	$ (722)
Net loss per ordinary share - basic and diluted	$ (0.45)	$ (0.68)	$ (2.31)	$ (5.07)	
Weighted average ordinary shares outstanding - basic and diluted	94,603,860	89,935,902	93,400,513	75,166,456	

Centessa Pharmaceuticals plc

Condensed Consolidated Balance Sheets
(unaudited)

(amounts in thousands)

	December 31, 2022	December 31, 2021
Total assets:		
Cash and cash equivalents	$ 393,644	$ 595,082
Other assets	50,663	34,553
Total assets	$ 444,307	$ 629,635
Total liabilities		
Other liabilities	$ 38,338	$ 24,681
Long term debt	69,800	75,700
Contingent value rights	—	37,700
Total liabilities	$ 108,138	$ 138,081
Total shareholders' equity	$ 336,169	$ 491,554
Total liabilities and shareholders' equity	$ 444,307	$ 629,635


CENTESSA
PHARMACEUTICALS
Corporate Overview
Asset-Centric. Patient-Centric.
April 2023

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, ORX750, MGX292 and our LockBody technology platform; strategy; regulatory matters, including the timing and likelihood of success of obtaining approvals to initiate or continue clinical trials or market any products; enroll subjects in clinical trials; 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: $393.6 million in cash and cash equivalents as of December 31, 2022.

DIFFERENTIATION

We are a transformational pharmaceutical company fueling an innovative pipeline

MULTIPLE PATHWAYS TO SIGNIFICANT VALUE CREATION

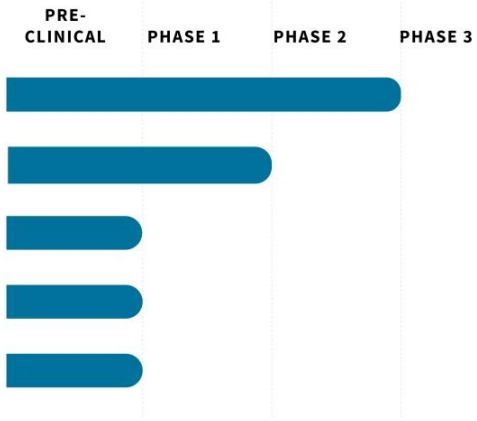
Lead Assets	Disease	Estimated Market Size*
SerpinPC	Hemophilia B	**$2B+**[1]
PD-L1xCD47 LockBody® (LB101)	Solid Tumors	**$10B**[1]
PD-L1xCD3 LockBody® Program	Solid Tumors	**$10B**[1]
ORX750	Narcolepsy (NT1) and other sleep disorders	**$2B+**[1]
MGX292	Pulmonary Arterial Hypertension (PAH)	**$6B**[1]

*Source: [1]Evaluate Pharma 2021 and internal estimates
Centessa has early- stage programs not reflected on this slide.

INNOVATIVE PIPELINE

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

ASSET	DISEASE	MECHANISM
SerpinPC	Hemophilia B	Activated Protein C Inhibitor
LB101	Solid Tumors	PD-L1xCD47 LockBody
Undisclosed	Solid Tumors	PD-L1xCD3 LockBody
ORX750	Narcolepsy Type 1 (NT1) and other sleep disorders	Orexin Receptor-2 (OX2R) Agonist
MGX292	Pulmonary Arterial Hypertension (PAH)	BMP9 Engineered Variant



CASH RUNWAY INTO 2026 ENABLES CLINICAL READOUTS ACROSS PIPELINE

CENTESSA PHARMACEUTICALS

Centessa has early-stage programs 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 · Deltinia · 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

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 DISCOVERIES · XO · McKinsey&Company · NOVARTIS

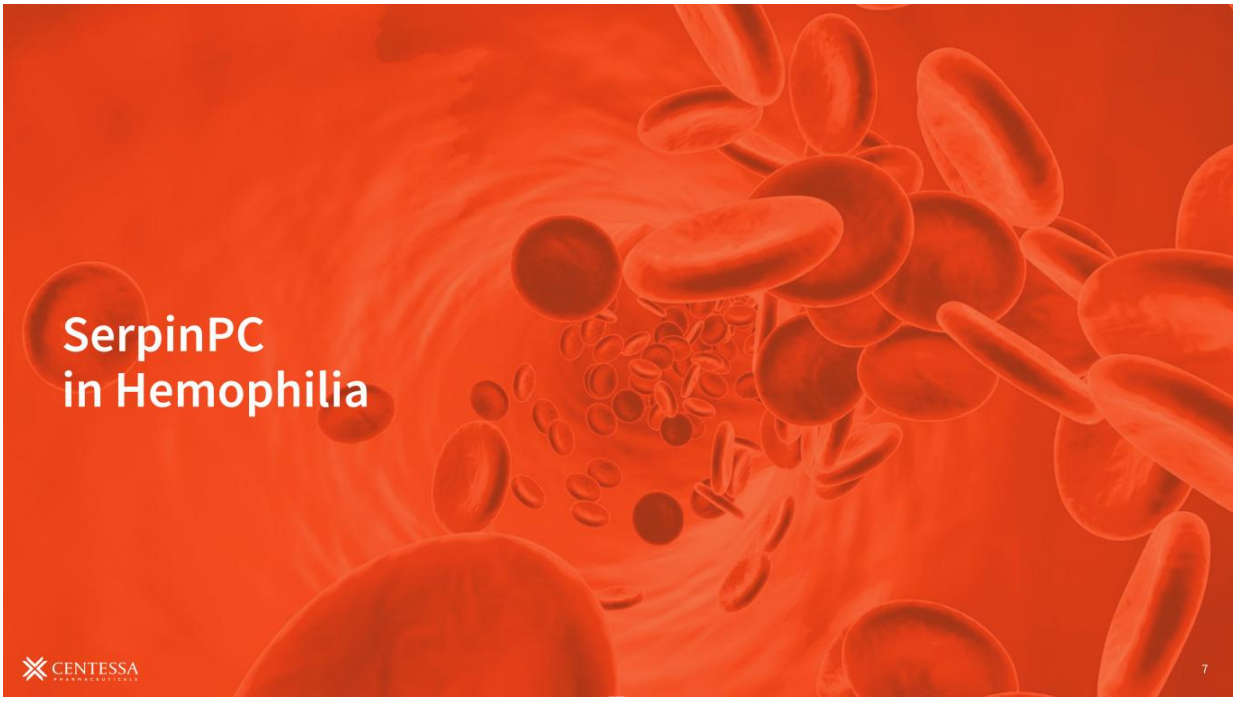
KAREN ANDERSON
Chief People Officer
Baxter · BAYER · Alnylam · Biogen · mimecast

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

HARRIS ROTMAN PhD
SVP, Regulatory Affairs
SANOFI · Shire · Wyeth · endo · SwanBio

PATRICK YUE MD
SVP, Clinical Development
GBT · GILEAD · PORTOLA

CENTESSA PHARMACEUTICALS


SerpinPC
in Hemophilia
CENTESSA
PHARMACEUTICALS
7

SerpinPC: Novel, subcutaneously administered biologic inhibitor of APC

In registrational program for the treatment of hemophilia B

HEMOPHILIA B UNMET NEED

Inconvenient, frequent and invasive IV dosing required with standard of care factor prophylaxis

Data for potentially competitive agents has shown potential risk of thrombosis

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

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

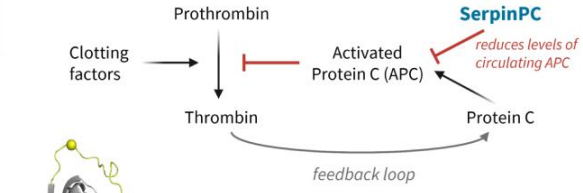
Shown to have a **favorable safety and well tolerated profile**[2]; **No thrombosis** observed[2]

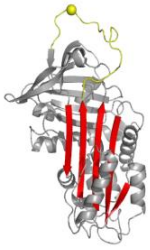
Designed as **convenient subcutaneous injection**

SerpinPC is an investigational serine protease inhibitor (SERPIN) engineered to specifically inhibit activated protein C (APC), that has not been approved by the FDA or any other regulatory authority. MoA is mechanism of action. *Source: 1. Evaluate Pharma 2021. 2. Phase 2a Study (AP-0101) 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.

SerpinPC: Designed to exploit novel pharmacology to prevent and reduce bleeding

Primary APC is the target of SerpinPC





3D-model of SerpinPC

Modified a1 anti-trypsin with 3 substitution mutations to confer selective inhibition of activated protein C (APC)

SerpinPC

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

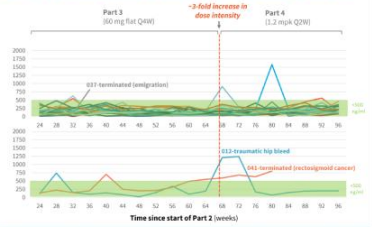
SerpinPC Phase 2a Study

Robust and highly differentiating clinical data

With total exposure of over 40 patient-years across multiple dosing regimens, Phase 2a data showed a continued favorable safety and tolerability profile for SerpinPC, as well as evidence of sustained efficacy, as measured by a reduction in the all-bleeds annualized bleeding rates (ABRs).

Favorable Safety Profile[1,2]

No observations of thrombosis or treatment-related, non-transient elevations in D-dimer[1,2]



The top graph shows the D-dimer results in the 17 subjects who had results < 500 and the 5 subjects who had non-consecutive results > 500. The bottom graph shows the results in the 2 subjects who had two or more consecutive results > 500. The blue line represents a subject who suffered a large traumatic hematoma (hip bleed), and the orange line represents a subject diagnosed with cancer, neither of which were determined to be treatment-related elevations.

Favorable Tolerability Profile[1]

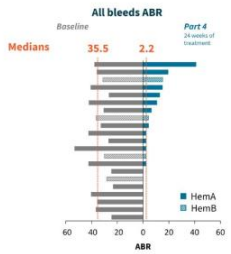
No observations of treatment-related, adverse events[1]

	Part 3 (n=22)		Part 4 (n=21)	
Treatment Emergent Adverse Events	Subjects with event No. (%)	Treatment-related*	Subjects with event No. (%)	Treatment-related*
Elevated ALT	3 (14%)	0	3 (14%)	0
Elevated gamma-GT	0	NA	2 (10%)	0
COVID-19 infection	2 (9%)	0	1	0
Hepatic fibrosis	1	0	1	0
Chronic hepatitis C	0	NA	1	0
Fever	0	NA	1	0
Urinary tract infection	0	NA	1	0
Fracture	1	0	1	0
Radiculopathy	1	0	1	0
Elevated creatinine phosphokinase	1	0	0	NA
Anemia	1	0	1	0
Elevated sodium	0	NA	1	0
Rectosigmoid cancer	0	NA	1	0
Low neutrophil count	1	0	0	NA

* Determined by Safety Review Group

Reduction in Bleeding[1]

SerpinPC reduced median all-bleed ABR by 93% at highest dose tested



Part 4 Dosing: 1.2 mpk of SerpinPC administered subcutaneously once every 2 weeks for 24 weeks

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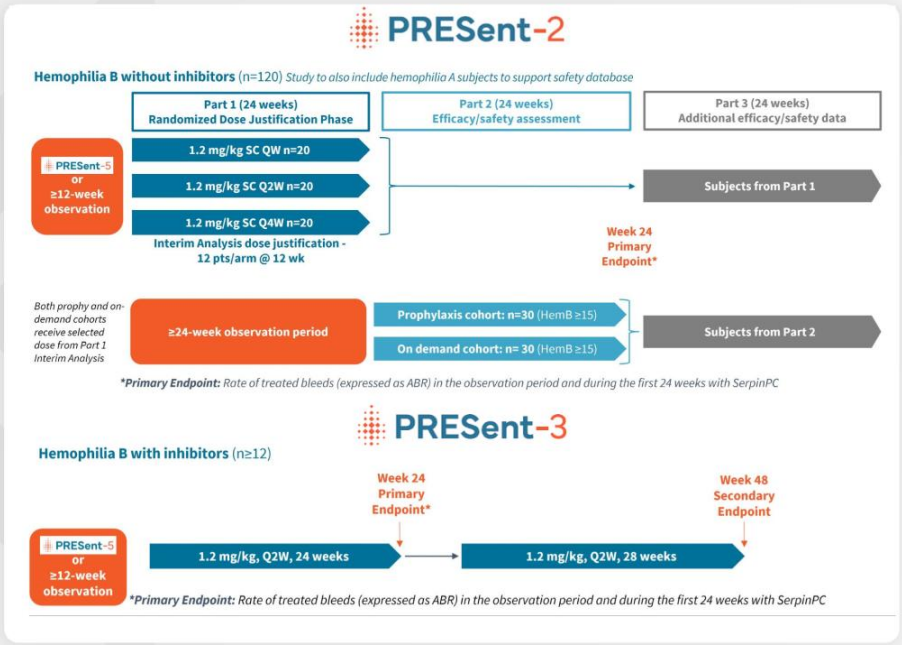
1. Phase 2a study data from Part 3 and Part 4 were presented in oral presentations at ASH and EAHAD in December 2022 and February 2023, respectively. 2. There were no thromboembolic events and no treatment-related sustained elevations of D-dimer observed across the Phase 2a study, to date. D-dimer is a sensitive measure of excessive thrombin generation.

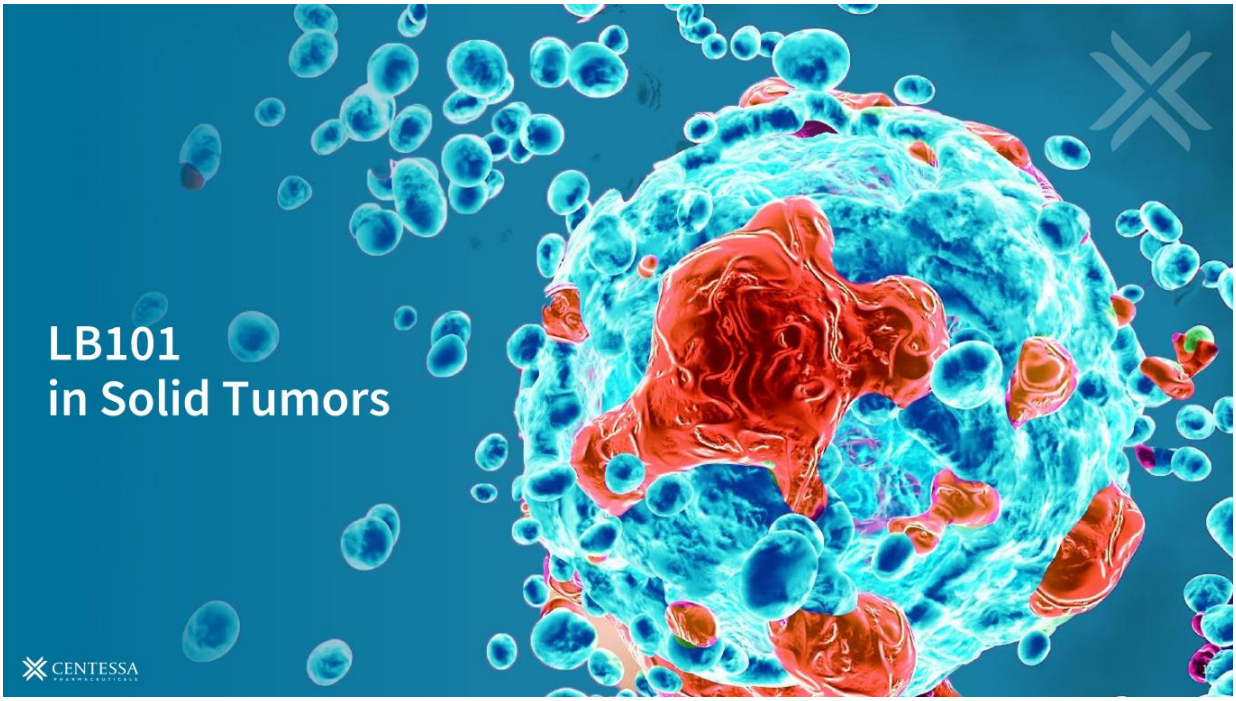
SerpinPC

In registrational program for hemophilia B, with and without inhibitors



CENTESSA PHARMACEUTICALS

SerpinPC has not been approved by the FDA or any other regulatory authority. Source: 1. Data from Phase 2a Study (AP-0101).

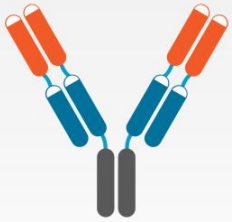

LB101
in Solid Tumors
CENTESSA

LB101: Novel, conditionally tetravalent PD-L1xCD47 bispecific monoclonal antibody

In Phase 1/2a first-in-human trial for the treatment of solid tumors

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

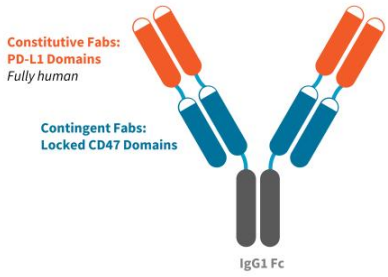
Robust non-clinical activity demonstrating potential **wide therapeutic index**

LB101, first candidate from modular **LockBody platform**

LB101 is an investigational agent that has not been approved by the FDA or any other regulatory authority. Company initiated Phase 1/2a clinical trial of LB101 and dosed first subject in March 2023.

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

LOCKED

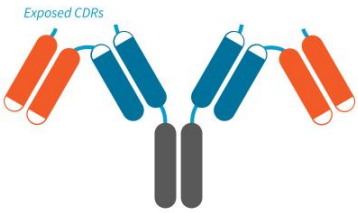


Peripheral Stability: IgG1 hinges naturally resistant to cleavage in serum

1. Constitutive Fabs drive tumor enrichment

2. Natural cleavage of IgG-derived hinges in tumors

UNLOCKED

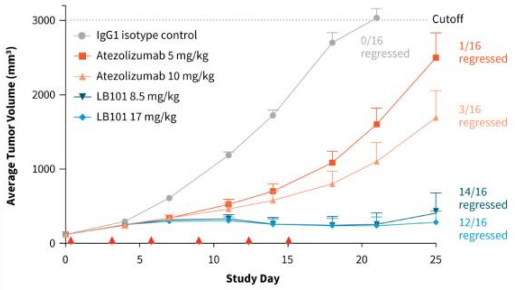


Tumor Unlocking: IgG1 hinges susceptible to cleavage in diseased tissue by various natural processes

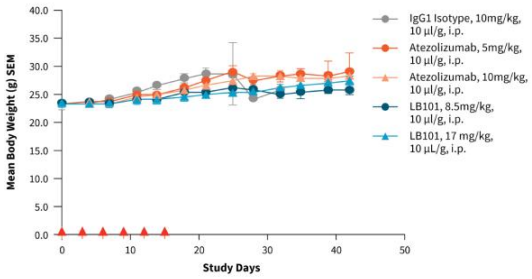
TME is tumor micro-environment

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



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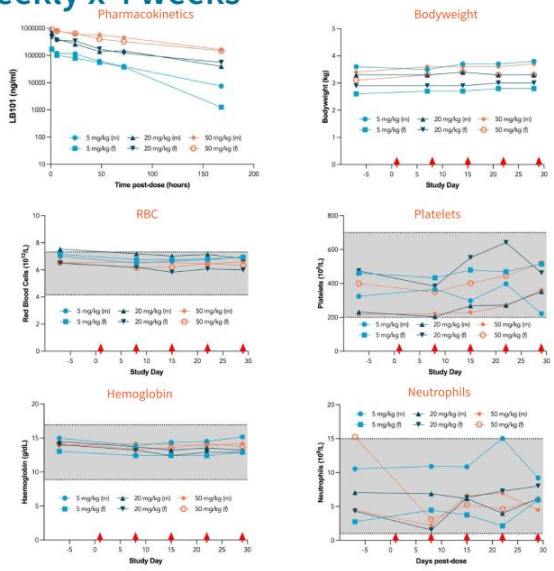
Note: MC38 hPD-L1+ syngeneic model in mouse; Arrows indicate dosing every 3 days (Q3d x 6) at Days 0, 3, 6, 9, 12, and 15. 5 mg/kg of atezolizumab is equivalent to 8.5 mg/kg of LB101.

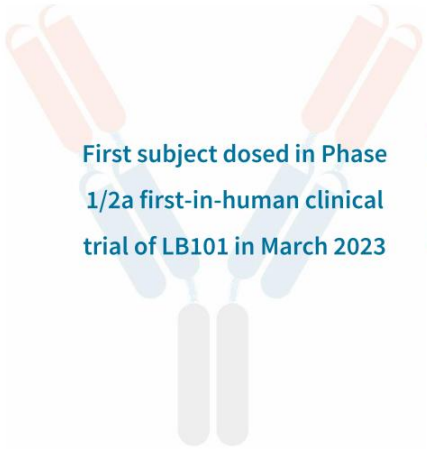
LB101 shown to have favorable safety and tolerability profile in non-human primates up to 50 mg/kg weekly x 4 weeks

***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



LB101 LockBody in Phase 1/2a Clinical Trial

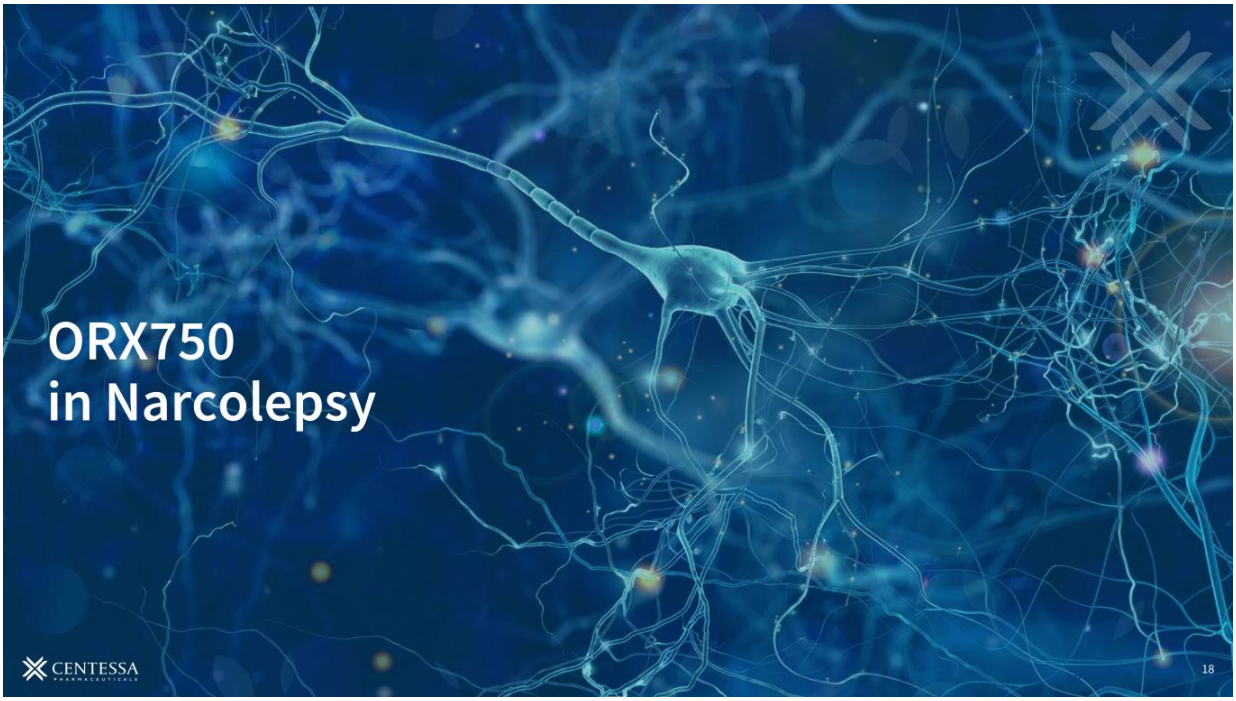


First subject dosed in Phase 1/2a first-in-human clinical trial of LB101 in March 2023

Phase 1/2a Clinical Trial

- Open-label, multicenter, dose escalation with expansion cohorts
- Part 1: LB101 **monotherapy** in subjects with selected, advanced solid tumors; determine recommended dose(s) for expansion (Part 2)
- Part 2: Design depends on Part 1 results; will further evaluate the safety, efficacy, tolerability, pharmacokinetics, and immune response of LB101
- Study to provide insights on LockBody technology platform in clinical setting

LB101 is an investigational agent that has not been approved by the FDA or any other regulatory authority. Company initiated Phase 1/2a clinical trial of LB101 in March 2023.


ORX750
in Narcolepsy
CENTESSA
PHARMACEUTICALS
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ORX750: orally administered, selective orexin receptor-2 (OX2R) agonist

In preclinical development for treatment of NT1; IND-enabling activities underway

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; symptoms persist despite polypharmacy

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

ORX750 designed to **reactivate orexin** signaling in the brain

Highly validated human target with clinical proof of concept in NT1

Molecule design allows for **potential expansion beyond NT1**

EDS is excessive daytime sleepiness. In March 2023, ORX750 was announced as the Company's product candidate for the treatment of NT1 with potential expansion into other sleep disorders. 1. Evaluate Pharma 2021. 2. Maski K, et al. J Clin Sleep Med 2017;13;419–25.

Structure-based drug design has enabled the discovery of ORX750 as potential orexin signaling ‘replacement therapy’ for NT1, with potential indication expansion beyond NT1

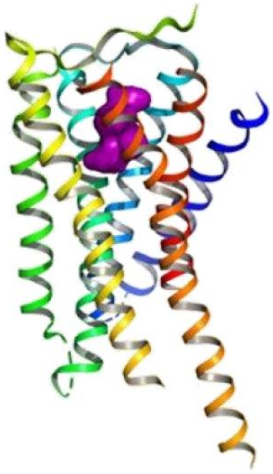

Illustration of OX2R structure
bound to prototype small molecule orexin agonist
(shown in purple)

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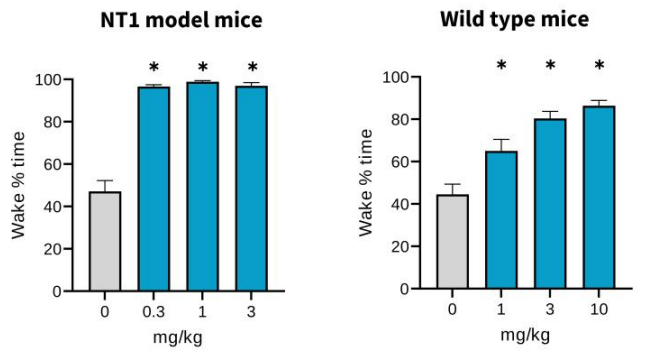
ORX750 increased wakefulness in NT1 model and wild type mice



ORX750 was dosed orally during the rest phase in the PiezoSleep assay; percent time spent awake in the first 2 h after dosing is quantified.

NT1 model shown here is orexin/ataxin-3 (Atax) mice, which recapitulates the degeneration of orexin neurons associated with NT1.

*P < 0.05 vs. 0 mg/kg

- ORX750 increased time awake in an NT1 mouse model, showing maximal wake promotion (ceiling effect) at doses shown
- Wake % time in wild type mice showed a dose-related response which supports potential indication expansion beyond NT1


MGX292 in
Pulmonary
Arterial
Hypertension
CENTESSA
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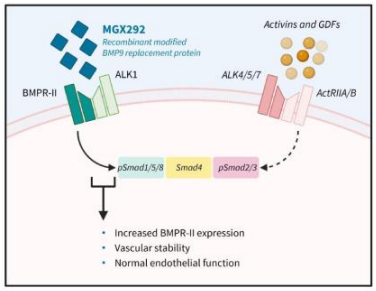
MGX292: Protein-engineered variant of BMP9, selective for BMPR2/ALK2

In preclinical development for treatment of PAH

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

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]

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*Source: 1. Evaluate Pharma 2021

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: $393.6 million in cash and cash equivalents as of December 31, 2022.


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