Creating transformative gene-based medicines for serious diseases

Corporate Overview

Q3 2025

Forward-Looking Statements

Statements contained in this presentation and other related materials regarding matters that are not historical facts are "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. Because such statements are subject to risks and uncertainties, actual results may differ materially from those expressed or implied by such forward-looking statements. Such statements include, but are not limited to, statements regarding any or all of the following: (i) CRISPR Therapeutics' preclinical studies, clinical trials and pipeline products and programs, including, without limitation, manufacturing capabilities, status of such studies and trials, potential expansion into new indications and expectations regarding data, safety and efficacy generally; (ii) data included in this presentation, as well as the ability to use data from ongoing and planned clinical trials for the design and initiation of further clinical trials; (iii) CRISPR Therapeutics' strategy, goals, anticipated financial performance and the sufficiency of its cash resources; (iv) plans and expectations for the commercialization of, and anticipated benefits of, CASGEVY, including anticipated patient access to CASGEVY; (v) regulatory submissions and authorizations, including timelines for and expectations regarding additional regulatory agency decisions; (vi) expected benefits of CRISPR Therapeutics' collaborations; and (vii) the therapeutic value, development, and commercial potential of gene editing technologies and therapies, including CRISPR/Cas9, as well as other technologies, and as compared to other therapies. Risks that contribute to the uncertain nature of the forward-looking statements include, without limitation, the risks and uncertainties discussed under the heading "Risk Factors" in CRISPR Therapeutics' most recent annual report on Form 10-K and in any other subsequent filings made by CRISPR Therapeutics with the U.S. Securities and Exchange Commission. Existing and prospective investors are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date they are made. CRISPR Therapeutics disclaims any obligation or undertaking to update or revise any forward-looking statements contained in this presentation and any related materials, other than to the extent required by law.

This presentation also contains estimates, projections, and/or other information regarding our industry, our business and the markets for certain of our product candidates, including data regarding the estimated size of those markets, and the incidence and prevalence of certain medical conditions. Unless otherwise expressly stated, we obtained this industry, business, market and other data from reports, research surveys, clinical trials, studies and similar data prepared by market research firms and other third parties, from industry, medical and general publications, and from government data and similar sources. Information that is based on estimates, forecasts, projections, market research, or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances reflected in this information.

This presentation and related materials discuss investigational therapies and is not intended to convey conclusions about efficacy or safety as to those investigational therapies or uses of such investigational therapies. There is no guarantee that any investigational therapy will successfully complete clinical development or gain approval from applicable regulatory authorities. Caution should be exercised when interpreting results from separate trials involving separate product candidates. There are differences in the clinical trial design, patient populations, and the product candidates themselves, and the results from the clinical trials of autologous products may have no interpretative value on our existing or future results.

CRISPR Therapeutics Today

Our vision is to develop cures for people suffering from serious diseases through transformative gene-based medicines

CASGEVY® for severe sickle cell disease and beta thalassemia enabled by Nobel-Prize winning CRISPR-Cas9 technology

Expanded portfolio into both common and rare diseases with de-risked underlying biology

Establish a sustainable industry-leading genomic medicines company

Executing on Our Vision Across Four Therapeutic Franchises

Heme

Partnered with Vertex on global launch of **CASGEVY, best-in-class, commercial *ex vivo* CRISPR-Cas9 therapy** for sickle cell disease and beta-thalassemia

Continued focus on **innovation to expand potential market** for CASGEVY

Advancing i*n vivo* approaches **leveraging LNP delivery**

CAR T

Best-in-class allogeneic cell therapies with novel potency edits

CTX112 demonstrates promising efficacy/safety profile in oncology

Expanding CTX112 into autoimmune disease to significantly increase value

Pipeline diversification with **CTX131** and **auto-GPC3 targeting solid tumors**

In vivo

Establishing a differentiated **LNP-mRNA platform**, initially focused on the liver

Two **Phase I programs (CTX310 and CTX320) in cardiovascular disease** to de-risk platform

CTX310 targeting ANGPTL3 has potential to benefit >40M patients in the U.S.

Building **extrahepatic** delivery and **next-gen editing** capabilities

T1D

Utilizing gene editing to develop an **allogeneic beta-cell replacement therapy** for diabetes

Goal to achieve **insulin independence without chronic immunosuppressive**

Advancing dual delivery strategies: device-based (CTX211) and deviceless (CTX213) approaches

Multi-target siRNA deal with Sirius Therapeutics includes lead asset SRSD107, a potential biannual siRNA targeting Factor XI entering Phase 2

Broad and Diversified Pipeline

HeFH: Heterozygous familial hypercholesterolemia; HoFH: Homozygous familial hypercholesterolemia; sHTG Severe hypertriglyceridemia SLE: Systemic Lupus Erythematosus; SSC: Systemic Sclerosis; IIM: Idiopathic Inflammatory Myopathies

[1] Currently approved in some countries for certain eligible patients with SCD or TDT; [2] Collaboration with Vertex for applications in TDT and SCD

Entering a Critical Phase of Our Growth Journey

Foundational Years

- Relentless focus to bring CASGEVY to global approval and launch
- Diversified into other therapeutic areas with multiple clinical candidates
- Operationalized in-house manufacturing capabilities

2020 - 2024

Inflection Year

- Strong launch trajectory for CASGEVY globally with favorable market access in SCD and TDT
- Clinical updates across core franchises including cardiovascular, immuno-oncology, and autoimmune
- Opportunistic business development across the portfolio exemplified by Sirius Therapeutics collaboration

2025

Sector-Leading Biotech

- CASGEVY revenue provides a path to a sustainable biotech company
- Clinical programs progress into later stages of development and potential approval
- Platform engine generating 1 to 2 new IND/CTAs annually
- Ongoing business development aligned with strategic priorities

2026+

Established efficient operating model and strong balance sheet of ~$1.72 billion[1]

[1] *As of June 30, 2025*

Hemoglobinopathies

2024: A Foundational Year for CASGEVY

Unparalleled speed and execution to a landmark approval[1]

casgevy™ (exagamglogene autotemcel) suspension for IV infusion

WSJ

FDA Approves World's First Crispr Gene-Editing Drug for Sickle-Cell Disease

Landmark decision heralds a new type of medicine that can tackle genetic conditions that are hard to treat

F.D.A. Approves Sickle Cell Treatments, Including One That Uses CRISPR

Addressable Market[2]

~60,000

Severe patients in approved territories eligible for treatment

Investments made to meet global demand for disease-modifying therapy

[1] Approved by the U.S. FDA for treatment of patients aged 12 years and older with sickle cell disease (SCD) with recurrent vaso occlusive crises (VOCs) and transfusion-dependent ß-thalassemia (TDT) Granted conditional marketing authorization by the UK MHRA and Bahrain NHRA for patients 12 years of age and older with SCD with recurrent VOCs or TDT for whom hematopoietic stem cell transplantation is appropriate and a human leukocyte antigen matched related hematopoietic stem cell donor is not available. CASGEVY has also been approved in other countries for certain eligible patients with SCD or TDT

[2] Including U.S., U.K., E.U., Kingdom of Saudi Arabia (KSA), Bahrain, Qatar, Canada, Switzerland, and United Arab Emirates (UAE)

2025: Focused on Execution and Expansion of Opportunity

Continued Progress in U.S. to Serve Significant Unmet Need

Cell and Gene Therapy Access Model

Rolling start for states: January 2025 to January 2026

New CMMI model to improve access and health outcomes, as well as reduce expenditures ($3B annual U.S. SCD cost)

Expanding into untapped Middle East and ex-U.S. Markets

Saudi Arabia Successfully Treats First Patient With Casgevy for Beta-Thalassemia

NHS

VISION رؤية 2030 المملكة العربية السعودية KINGDOM OF SAUDI ARABIA

First GCC patient reimbursed at ~$2M; NHS reimbursement achieved for beta-thal.

Manufacturing Expansion to Support Launch[1]

Commercial agreement to manufacture CASGEVY®

Lonza

Manufacturing agreement for global commercial supply with Lonza

As of June 30th 2025, CASGEVY is approved in 10 jurisdictions, >75 authorized treatment centers (ATCs) have been activated globally and ~115 patients have initiated cell collection

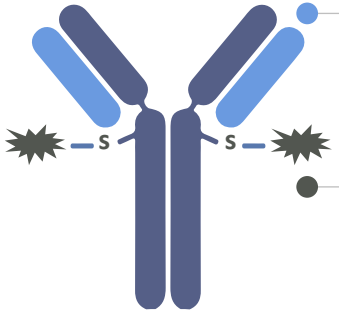
CMMI: Center for Medicare and Medicaid Innovation; GCC: Gulf Cooperation Council

[1] Vertex leads development, regulatory filings, manufacturing and commercialization

Serial Innovation in Enabling Technologies to Broaden Access

Targeted conditioning

cKit (CD117) antibody-drug conjugate (ADC) for specific depletion of hematopoietic stem cells (HSCs) and no off-target/bystander toxicity



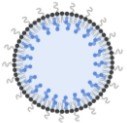
- Proprietary **GMP monoclonal antibody** with **short half-life** to enable rapid infusion of edited cells
- Validated **GMP toxin** with HSC activity and **reduced hydrophobicity** to limit non-target cell toxicity

Studies in non-human primates (NHP) ongoing

150k+ addressable patients worldwide

In vivo editing of HSCs

DELIVERY | **EDITING**

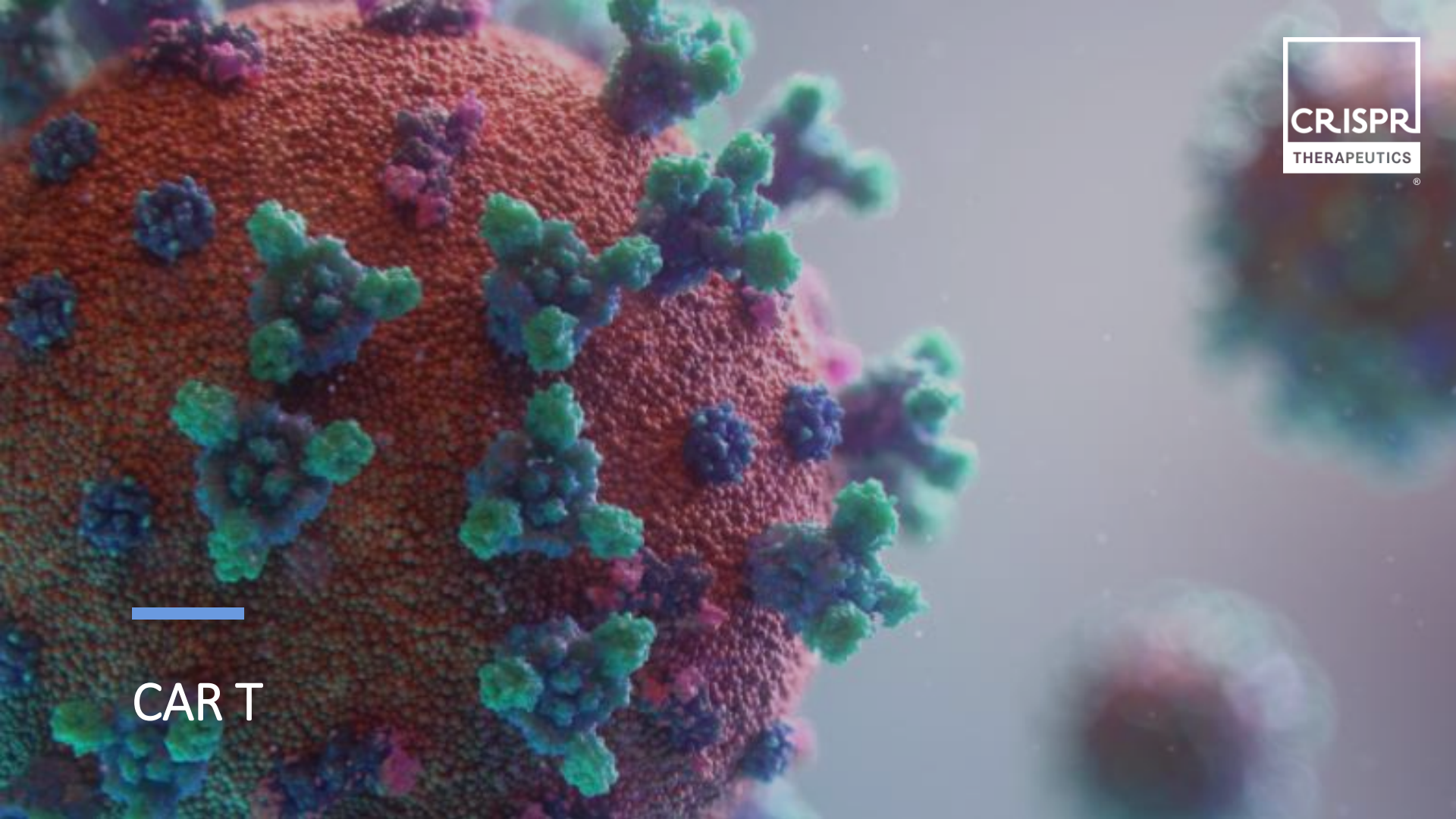


Creating optimized system for *in vivo* HSC editing with ideal characteristics, including:

- **Tolerable doses with no off-target toxicities**
- **Editing of LT-HSCs for durable effects vs. HSPCs only**
- **Potential for redosability to enhance editing**

Core research focus in 2025 – NHP studies ongoing

400k+ addressable patients worldwide



CAR T

Best-in-Class Cell Therapy Platform for Treating Cancer and Autoimmune Disease

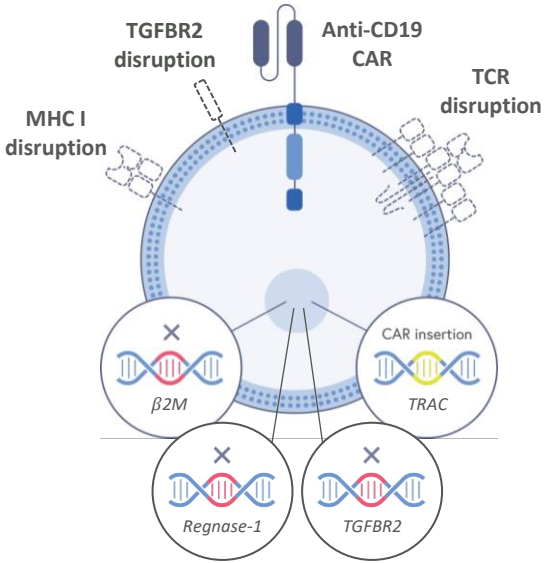
CTX112	CTX131	Autologous GPC3
Currently in Phase I/II trial in r/r NHL, plus Phase I trial in SLE/SSc/IIM	Currently in Phase I/II trial in RCC, plus Phase I/II trial in TCL	Ongoing preclinical work with anti-GPC3 autologous CAR T with TGFBR2 KO
Update 2H 2025	**Update in 2025**	**IND accepted and trial open**

Program	Indication(s)	Research	IND-enabling	Clinical	Partner
CTX112 Anti-CD19 allogeneic CAR T	B cell malignancies				
	SLE/SSc/IIM				
CTX131 Anti-CD70 allogeneic CAR T	Renal cell carcinoma and other solid tumors				
	Hematological cancers				
Anti-GPC3 Autologous CAR T	Hepatocellular carcinoma				ROSWELL PARK

SLE: Systemic Lupus Erythematosus; SSC: Systemic Sclerosis; IIM: Idiopathic Inflammatory Myopathies; TCL: T Cell lymphoma; GPC3: Glypican-3; TGFBR2: Transforming Growth Factor Beta Receptor Type 2

CTX112: An Allogeneic CAR T Optimized for Potency

CTX112 Novel Potency Edits (TGFBR2, Regnase-1)



Regnase-1 and TGFBR2 edits synergistically increase CAR T potency

Other CTX112 Competitive Advantages

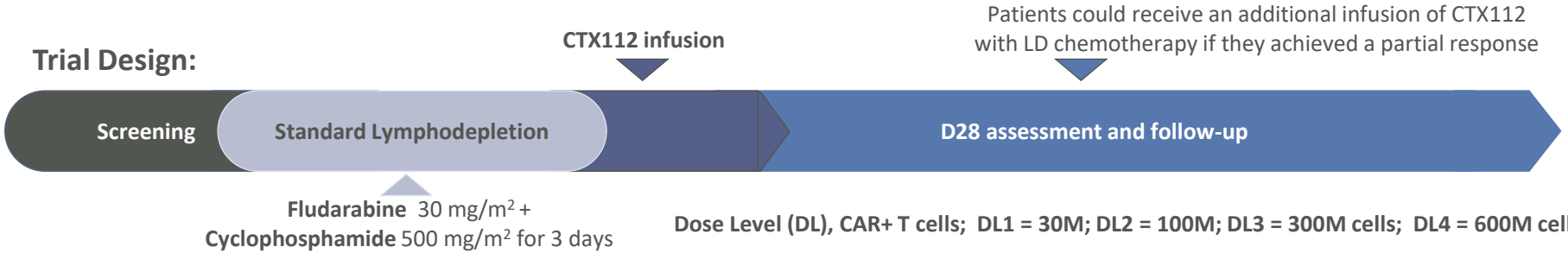
- Ability to multiplex gene edits precisely and efficiently
- Comprehensive and FDA-validated genomic analysis
- Scalability and low COGS to enable global expansion
- In-house manufacturing enables direct control over process and timelines

Multiple scientific, manufacturing and regulatory advantages for CTX112

CTX112 Phase I Immuno-Oncology Clinical Trial Design

Open-label, multicenter, Phase I/II study evaluating the safety and efficacy of CTX112 in relapsed or refractory B-cell malignancies

Trial Design:



Benefits of Allogeneic CAR T:

- Short screening timeframe
- No apheresis
- No bridging chemotherapy
- On-site availability of CAR T cell product

Key eligibility criteria:

- Age ≥18 years
- Patient population: R/R FL grade 1-3a, MZL, MCL, DLBCL NOS, DLBCL/high- grade lymphoma with MYC and BCL-2 rearrangement, grade 3b FL, DLBCL arising from FL or MZL or LBCL with prior CAR T
- No prior allogeneic SCT and no history of CNS lymphoma involvement
- Adequate organ function

Primary endpoint

- Incidence of AEs, defined as DLTs
- ORR (per Lugano 2014 criteria or iwCLL 2018 guidelines for CLL/SLL)

Secondary endpoints

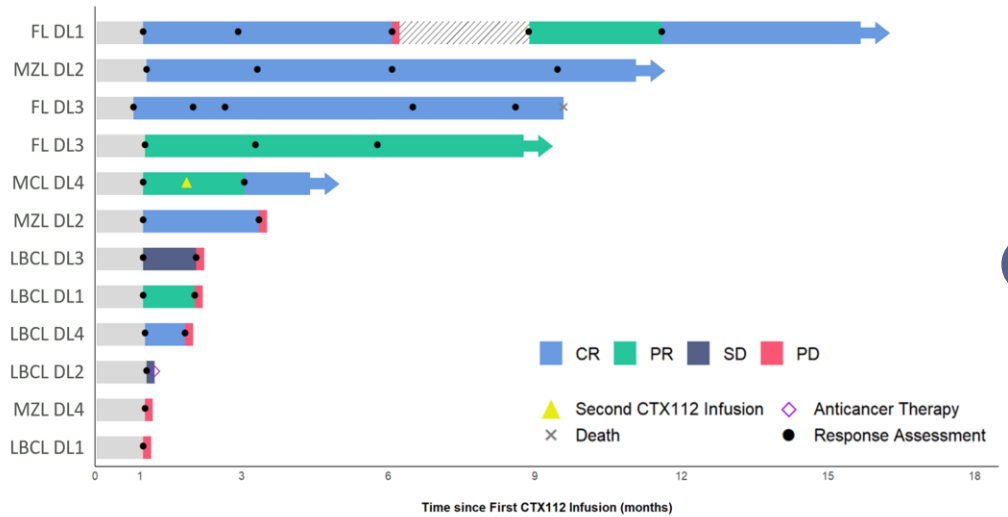
- CR rate
- Duration of response (DOR)
- Progression-free survival (PFS)
- Overall survival

(NCT05643742); AE, adverse event; BCL-2, B-cell lymphoma 2; CNS, central nervous system; DLT, dose-limiting toxicity; iwCLL, International Workshop on CLL; ORR, overall response rate; R/R, relapsed or refractory; SCT, stem cell therapy.

Initial Efficacy Data On Par with Auto CAR T

CTX112 Initial Efficacy Data (N=12)
High risk patient population (58% primary refractory; 67% >3 prior therapies; 50% with tumor SPD > 4000 mm2)
CTX112 demonstrated tolerability with no CRS, ICANS or infections Grade ≥3

Patient-level data



Ongoing Responses in Patients with Poor Prognostic Factors

Aggregated data per dose level

Cell dose (CAR+ T cells)	DL1 30M N=3	DL2 100M N=3	DL3 300M N=3	DL4 600M N=3	Total N=12
ORR n (%)	2 (67)	2 (67)	2 (67)	2 (67)	**8 (67)**
CR n (%)	1 (33)	2 (67)	1 (33)	2 (67)	**6 (50)**
PR n (%)	1 (33)	0	1 (33)	0	**2 (17)**

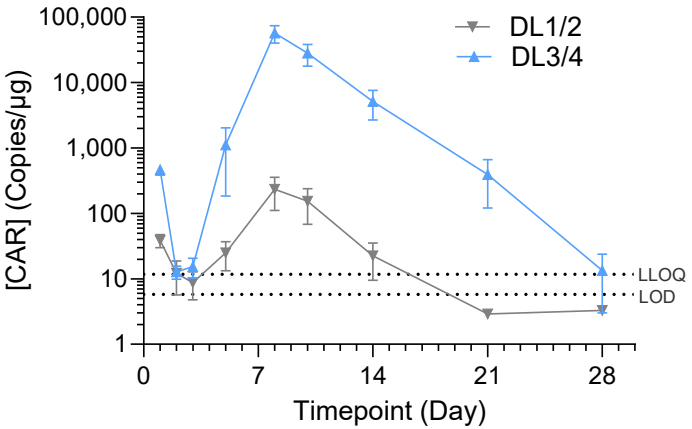
ORR/CR rate in line with approved autologous CAR T[1]

Data published at 2024 American Society of Hematology Annual Meeting
[1] For example, Yescarta ORR/CRR 70-90%/50-60% across indications. Response rates based on modified intent to treat analyses of infused patients in the Zuma-1 and Zuma-5 trials

Updated CTX112 Data Shows PK in Line with Auto CAR T

Analysis from subsequent data cut on Dec 20, 2024 (N=25)

CTX112 Cell Expansion Data



Dose Dependent Increases in AUC and C_{max}

CAR T Cell Expansion Comparison

	CTX112 (DL3/4)	Autologous CAR T	Other Allogeneic CAR T
Mean C_{max} (copies/µg)	45,000-70,000[1]	Apx. 6,000-30,000[2]	Apx. 500-5,000[3]

Cell expansion comparable to autologous CAR T[2]

[1] Mean +/- the SEM; [2] Per Kymriah and Breyanzi USPI; [3] Lekakis et al. ASH 2021, Hu et al. ASCO 2024

Updated CTX112 Data Shows Efficacy in post-TCE Subset

Analysis from subsequent data cut on Dec 20, 2024

	Histology	# Prior Lines	Prior Bispecific T Cell Engager (TCE)	TCE Best Overall Response	CTX112 Best Overall Response
Dose level 3	FL	7	5L: Mosunetuzumab	PR	PR
	LBCL	2	2L: R-ICE & Epcoritamab	PD	PR
	LBCL	10	5L: Mosunetuzumab	UNK	PR
			6L: Tafasitamab & Rituximab & Lenalidomide	PD	
Dose Level 4	LBCL	4	4L: Epcoritamab & GemOx	CR	CR
	FL	8	7L: Imvotamab (IGM-2323)	PD	CR
	FL	5	3L: Glofitamab & RG6333 (CD19/CD28)	PR	CR

100% overall response rate (ORR) for 6 patients receiving CTX112 post-TCE therapy
100% ORR for 3 LBCL patients at higher dose levels

TCE: T-cell engager; FL: follicular lymphoma; LBCL: Large B-cell lymphoma

CTX112 is Positively Differentiated From Other CD19 Therapies

CTX112 vs. Autologous CAR T	• **Safety benefits** are critical in context of larger patient populations and in community hospital settings • **Improved patient experience** with no apheresis; enables rapid enrollment to dosing without the need to pause immunosuppressants • **Significantly lower COGS and scalability** are critical for expanding the addressable population
CTX112 vs. TCE	• **Initial clinical results with CAR Ts show deep B-cell depletion in tissues**, likely critical for immune reset • **Long-term data in oncology supports more durable clinical responses** with CAR T therapy vs. TCEs • Initial **CTX112 data shows promising efficacy in post-TCE patients** (e.g., 100% OR rate)
CTX112 vs. Other Allogeneic CAR T / NK	• **Case studies** from other allogeneic CAR T therapies in AID **provide derisking for CTX112** • CTX112 may be superior, with potency edits leading to **significantly higher CAR T cell expansion and functional persistence**

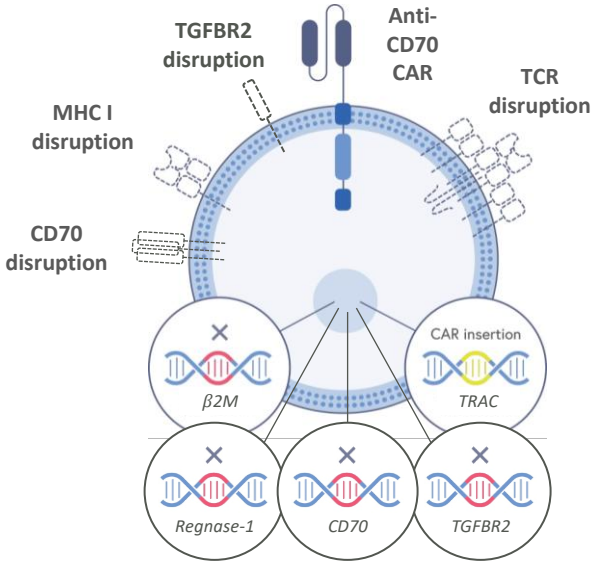
Broad CTX112 update across Oncology and Autoimmune disease expected in 2H 2025

Next-Generation CAR T for Solid Tumors

Solid Tumor CAR T pipeline

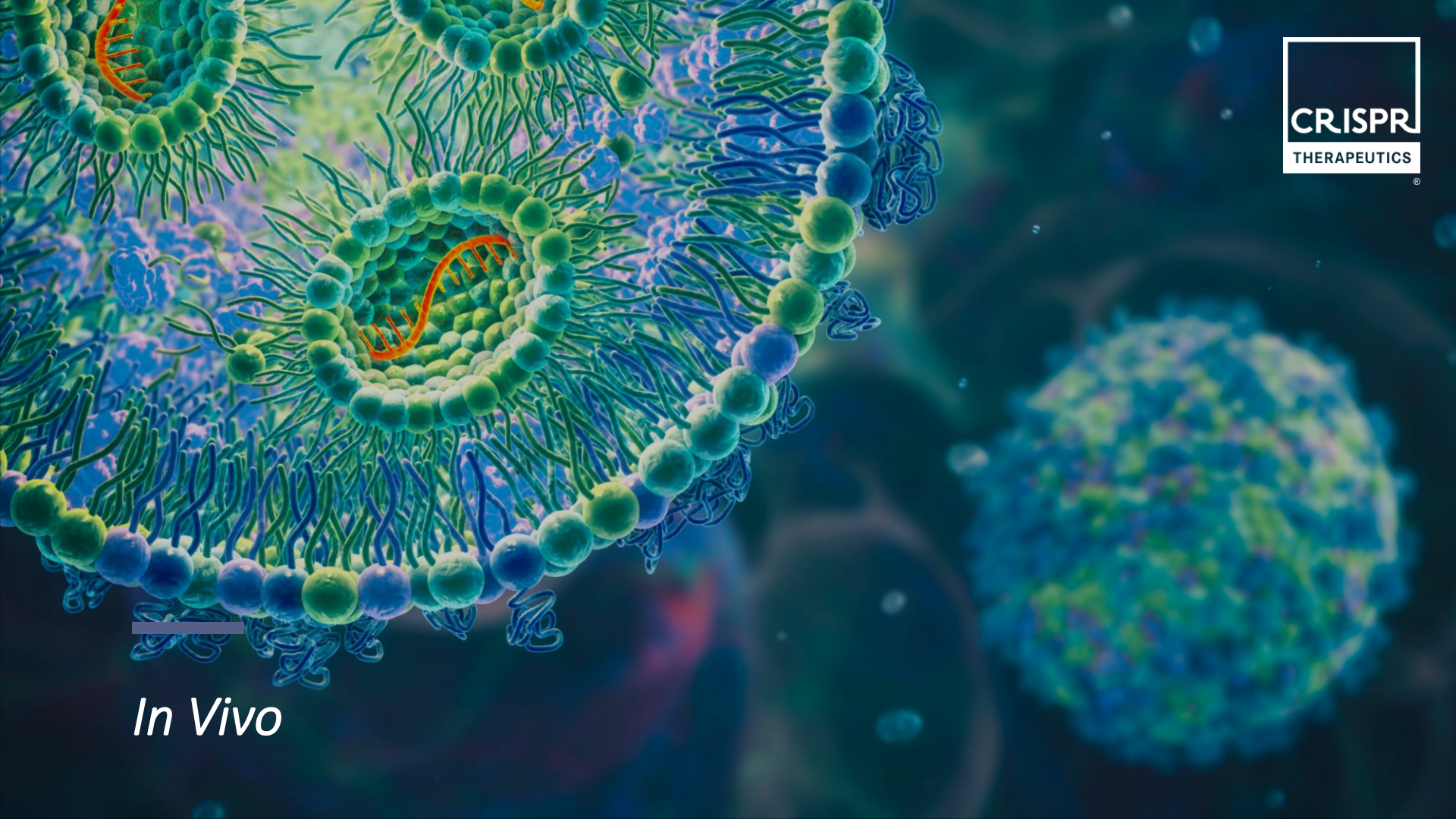
Program	Indications
CTX131 Anti-CD70 allogeneic CAR T	▪ **Phase I trial in RCC** and other solid tumors ongoing; update in 2025 ▪ **Phase I trial in hematologic malignancies, including T cell lymphomas (TCL)** dose escalation ongoing
Anti-GPC3 autologous CAR T with TGFBR2 KO	▪ **IND accepted and trial open for Phase I in HCC** ▪ **TGFB edit prevents exhaustion**; validating data from China clinical trials ▪ **Roswell Park** conducts manufacturing and clinical trial; CRISPR has commercial rights

CTX131 Next-Generation CAR T Chassis: Most sophisticated allogeneic CAR T candidate in the clinic



Regnase-1 and TGFBR2 edits synergistically increase CAR T potency

RCC: renal cell carcinoma; HCC: Hepatocellular carcinoma carcinoma



In Vivo

Plug-and-play LNP/mRNA Platform for Gene Disruption

CTX310

ANGPTL3 targeted asset with potential across multiple indications

Update in 2H 2025

CTX320

Potential to address large patient populations with elevated Lp(a)

Update in 1H 2026

CTX340/450

Additional preclinical programs targeting AGT and ALAS1 respectively

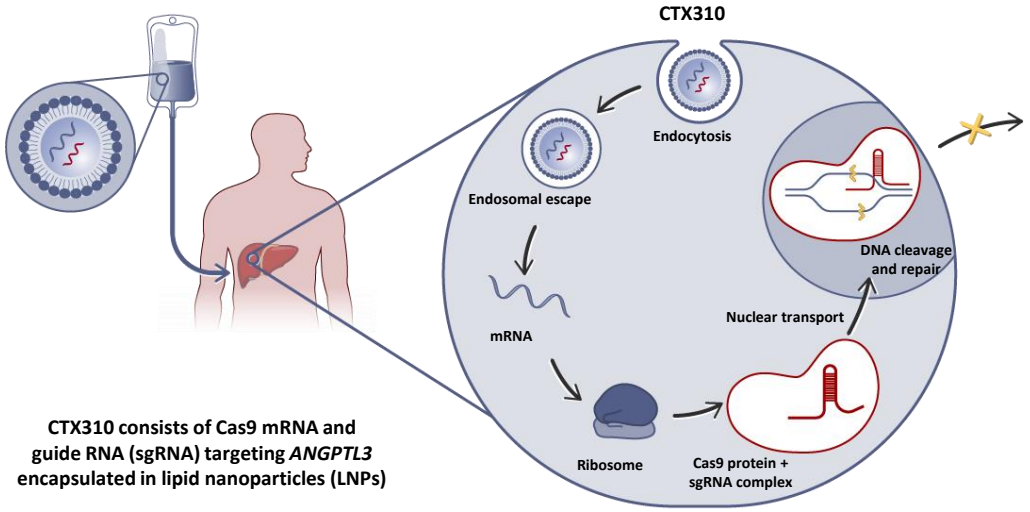
Progressing to IND/CTA

Program	Indication(s)	Research	IND-enabling	Clinical
CTX310: ANGPTL3	HeFH[1], HoFH[2], Mixed dyslipidemias, and sHTG[3]	●	●	●
CTX320: Lp(a)	ASCVD with elevated Lp(a)	●	●	●
CTX340: AGT	Refractory hypertension	●	●	○
CTX450: ALAS1	Acute hepatic porphyria	●	●	○

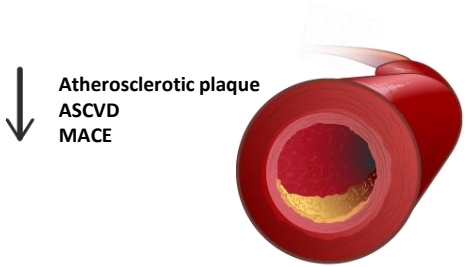
[1] Heterozygous familial hypercholesterolemia; [2] Homozygous familial hypercholesterolemia; [3] Severe hypertriglyceridemia

CTX310: A One-Time Therapy to Silence Expression of ANGPTL3

Intravenous delivery targeting the liver → **CRISPR/Cas9-based editing of *ANGPTL3*** → **Reduced atherogenic lipoprotein concentrations**



CTX310 consists of Cas9 mRNA and guide RNA (sgRNA) targeting *ANGPTL3* encapsulated in lipid nanoparticles (LNPs)



Transient expression of Cas9 and sgRNA in hepatocytes to reduce ANGPTL3 expression permanently

Unlike other targets (e.g., PCSK9, APOC3), ANGPTL3 can simultaneously address elevated LDL/TG

Low-density lipoprotein cholesterol (LDL-C); Triglycerides (TG)

Phase I Study Evaluating the Safety and Efficacy of CTX310

Open-label, multicenter, Phase Ia/Ib study evaluating the safety and efficacy of CTX310 in homozygous familial hypercholesterolemia (HoFH), heterozygous familial hypercholesterolemia (HeFH), severe hypertriglyceridemia (sHTG), or mixed dyslipidemias

Phase Ia: Single ascending dose escalation to identify optimal biological dose

- DL4 – 0.8mg/kg
- DL3 – 0.6mg/kg
- DL2 – 0.3mg/kg
- DL1 – 0.1mg/kg

Key eligibility criteria

- Age ≥18-75 years
- TG (>300 mg/dL) and/or LDL-C (>100 mg/dL); >70 mg/dL for subjects with ASCVD
- No significant comorbidities

Key Objectives/Endpoints

- Safety and Tolerability
- Preliminary efficacy including changes in ANGPTL3, LDL, TG and ApoB compared to baseline
- Pharmacokinetics

Phase Ib

- Patients with refractory hypercholesterolemia and or hypertriglyceridemia
- Phase Ib dose informed by Phase Ia

Dose Level (DL); Estimated lean body weight-based doses

Initial Results for CTX310 Phase 1 Dose Escalation Trial

N=10; data cutoff April 16, 2025

	Mean % Change from Baseline at Day 30 post-infusion (+/- SEM)		
Dose Level (DL)	**0.1 + 0.3 mg/kg (n=6)**	**0.6 mg/kg (n=3)**	**0.8 mg/kg (n=1)**
Patient type	HeFH(4), MDL, sHTG	MDL(2), HeFH	sHTG
Triglycerides	-10.6% ± 13.1%	-55.7% ± 8.0%	-81.9%
LDL	34.8% ± 27.0%	-28.5% ± 24.4%	-64.6%

Efficacy Highlights

- 0.8 mg/kg (DL4) patient with sHTG had an 82% reduction in triglycerides from a baseline of 1073 mg/dL at day 30
- 0.6 mg/kg (DL3) patient with HeFH had an 81% reduction in LDL-C from a baseline of 256 mg/dL at day 90

Safety Highlights

- No treatment-related severe adverse events (SAEs) and no grade ≥3 adverse events (AEs)
- No clinically significant changes in ALT, AST, bilirubin, or platelets any dose level

All dose levels well tolerated - no dose dependent trend in any lab measure

Alanine aminotransferase (ALT); Aspartate aminotransferase (AST); mixed dyslipidemia (MDL), heterozygous familial hypercholestrolemia (HeFH), severe hypertriglyceridemia (sHTG)

Large Addressable Patient Population for CTX310

HoFH	HeFH	Mixed dyslipidemias	sHTG
▪ LDL-C can reach >400 mg/dL	▪ LDL-C can reach >190 mg/dL	▪ Adults with high LDL-C and TG 150-499 mg/dL	▪ Adults with ≥500 mg/dL fasting triglyceride levels
~1.5K U.S. Patients[1]	**~1M U.S. Patients[2]**	**>40M U.S. Patients[3]**	**~3M U.S. Patients[4]**

Increasing LDL-Cholesterol

Increasing Triglycerides

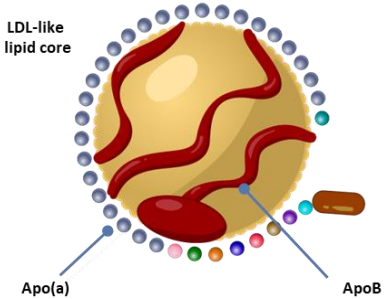
>40M U.S. patients affected by elevated LDL, severely elevated TGs or both; CTX310 initially focused on high-risk patient subset with greatest unmet need

[1] Cuchel et al. 2023; [2] Ferranti et al. 2016; [3] Tóth et al. 2012; [4] Miller et al. 2011
Low-density lipoprotein cholesterol (LDL-C); Triglycerides (TG)

Lp(a): An Emerging Key Target to Potentially Reduce CV Events

Lp(a) is an independent risk factor for atherosclerotic cardiovascular disease (ASCVD)

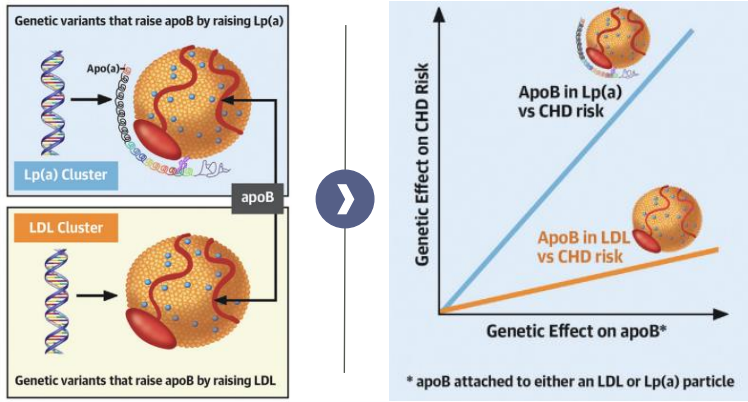
Lp(a) contains a single apo(a) molecule covalently bound by a disulfide bridge to ApoB



Apo(a) is encoded by the *LPA* gene and determines plasma Lp(a) levels

- Lp(a) is an LDL-like lipoprotein synthesized and secreted by hepatocytes
- Epidemiologic, Mendelian randomization, and genome-wide association studies have shown that elevated Lp(a) levels increase ASCVD risk[1,2,3]
- The genetic risk associated with elevated Lp(a) is cumulative over a person's lifetime and cannot be adequately reduced by lifestyle changes or currently approved therapies

Comparison of atherogenicity of Lp(a) and LDL

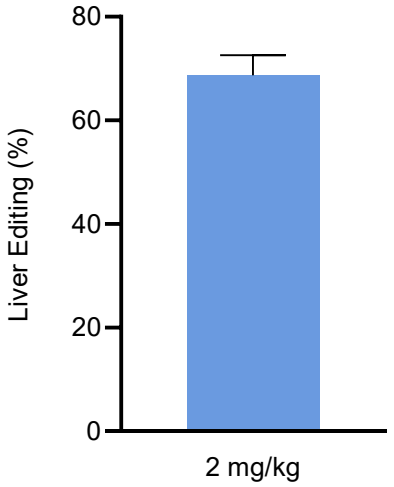


Lp(a) is 6x more atherogenic than LDL on a per-particle basis[4], highlighting Lp(a) as a key target for drug-based intervention

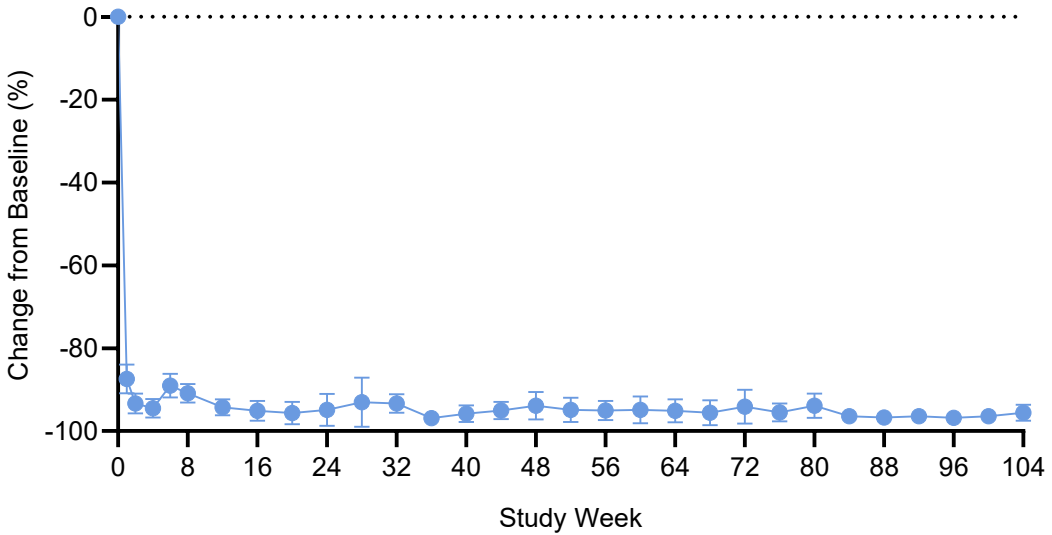
Lp(a): lipoprotein(a); [1] Enas et al. 2019; [2] Gurdasani et al. 2012; [3] Laschkolnig et al. 2014; [4] Björnson et al. 2024

Single CTX320 Dose Resulted in Durable Lp(a) Reduction (NHP)

~70% editing of *LPA*[1] at 1 year



~95% reduction in plasma Lp(a) sustained at 2 years



Updated NHP data demonstrate continued durability of CTX320 out to 2 years

Single dose of CTX320 (2 mg/kg) administered to NHPs (N=4) on Day 1; Editing data presented at the American Heart Association Scientific Sessions. 11 Nov 2023; Editing rate reflects whole liver editing

[1] LPA gene encodes apolipoprotein(a), a key component of lipoprotein(a)

Phase I Study Evaluating the Safety and Efficacy of CTX320

Phase I: Single ascending dose escalation to identify optimal biological dose

- Dose level 4
- Dose level 3
- Dose level 2
- Dose level 1

Key eligibility criteria

- Age ≥18-65 years
- Elevated levels of Lp(a) (>200nmol/l) and CVD
- Adequate renal, liver, cardiac, and pulmonary organ function
- No significant comorbidities

Objectives/Endpoints

- Safety and Tolerability
- Change in Lp(a) compared to baseline
- Pharmacokinetics

Phase II

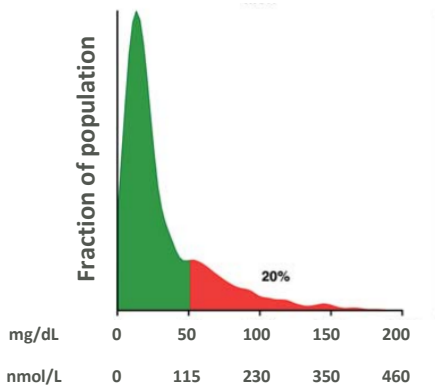
- Patients with elevated levels of Lp(a)
- Phase II dose informed by Phase I

CTX320 update in 1H 2026

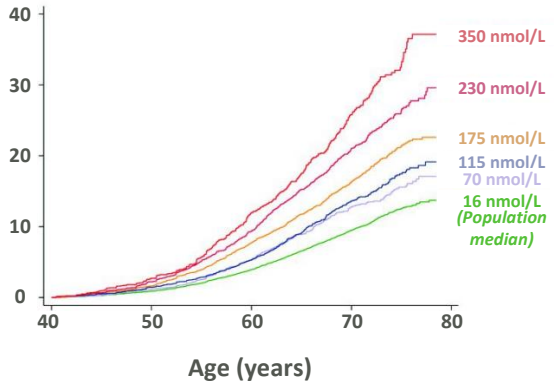
CTX320 Has Potential to Address Population with Elevated Lp(a)

Elevated Lp(a) is considered the most common genetically inherited risk factor for cardiovascular disease (CVD)[1]

Distribution of Lp(a) levels in general population[2]



Lifetime risk of major cardiovascular events with increasing Lp(a) levels[3]



Approximately one-fifth of the global population have elevated Lp(a) levels ~3x greater lifetime risk for most elevated Lp(a) population

A one-time durable reduction in Lp(a) has the potential to transform the current treatment paradigm in cardiovascular disease (compliance with small molecules and mAbs remains key issue)

siRNA cardiovascular outcomes trials in 2025/2026 have the potential to significantly de-risk Lp(a) as a therapeutic target

CTX320 has potential to benefit >60M U.S. patients with elevated Lp(a)

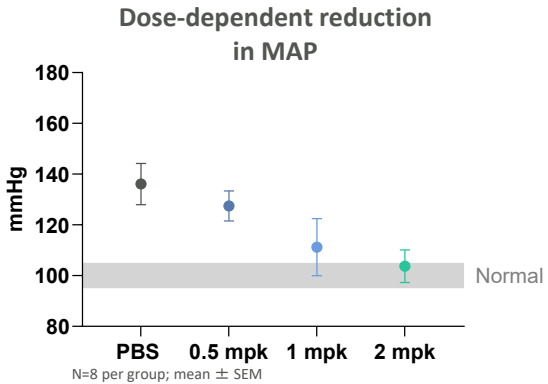
Population Lp(a) level based on male distribution; similar distribution seen across women

[1] Madsen et al. 2020; [2] Nordestgaard et al. 2010; [3] Kronenberg et al. 2022

Two Additional Programs Advancing Toward Clinic

CTX340 Targeting AGT For Refractory Hypertension

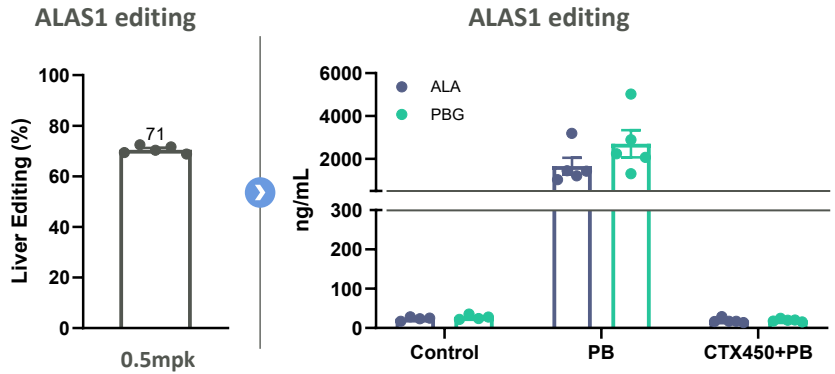
- Hypertension is the leading cause of cardiovascular morbidity and mortality worldwide[1,2]
- By going upstream of typical therapeutic approaches by targeting AGT, we can significantly impact hypertension and reduce dependence on other antihypertensives



Dose-dependent, durable reduction in blood pressure in SHR model

CTX450 Targeting ALAS1 for AHPs

- Acute hepatic porphyrias (AHP) are caused by deficiencies of specific enzymes in the heme biosynthesis pathway leading to the build-up of toxic metabolites[3,4]
- By targeting the upstream enzyme ALAS1 we can significantly reduce the production of these metabolites (e.g., ALA, PBG)



N=5 per group; mean ±SEM

~70% editing of ALAS1 Leading to reduction of ALA and PBG biomarkers in PB challenge model

Editing rates reflect whole liver editing; MAP: mean arterial pressure; SHR: spontaneous hypertensive rat; ALA: Aminolevulinic acid; PBG: porphobilinogen; PB: phenobarbital (PB)

[1] Zhou et al. 2021; [2] Danaei et al. 2009; [3] Anderson et al. 2001; [4] Chan et al. 2015

Three Parallel Efforts in Type 1 Diabetes (T1D)

Gene editing is key to achieving the goal of developing a beta-cell replacement product to treat diabetes without requiring long-term immunosuppression

1

CTX211

First-in-class edited beta-cell replacement therapy

Encapsulated pancreatic progenitor cells derived from pluripotent stem cells with gene-edits for immune evasion and cell survival

Phase I clinical trial

2

CTX213

Deviceless, iPS-derived, edited beta-cell replacement therapy

Pancreatic progenitor cells derived from edited pluripotent stem cells directly infused vs. delivered via device

Advancing into IND-enabling phase

3

Non-exclusive license with Vertex

Covers Vertex's gene-edited hypoimmune programs for T1D

$170M in upfront and milestone payments to CRISPR in 2023

Up to $160M in additional research and development milestones, plus royalties on future products

T1D update in 2025

Next-Generation Editing and Proprietary LNP Platform

The race to bring next-generation gene-editing technologies to the clinic has only just begun

Both editing and delivery expertise are needed to make the required edit at the required location

No single editing approach will dominate; each disease will require its own optimal strategy

Dedicated internal research group focused on emerging technologies for gene correction and insertion, including non-viral DNA delivery and all-RNA systems

Dedicated LNP group supporting liver-directed and extrahepatic *in vivo* programs with novel lipids and formulations, targeting moieties, etc.

Most next-generation editing technologies combine the RNA-guided endonuclease activity of Cas9 with a fused effector domain, e.g., a reverse transcriptase – **we have issued foundational IP covering such fusions**

2025: A Year of Significant Value Creation

Ongoing launch of **CASGEVY** with investments driven by strong patient demand

Catalyst rich year with several data readouts expected across our pipeline:

- CTX112 update in Oncology and Autoimmune diseases in the second half of 2025
- CTX310 update in the second half of 2025
- Additional updates across our pipeline, including CTX131 and T1D

Strong balance sheet with clear path toward building a sustainable biotechnology company

Opportunities for **additional business development across our portfolio**