43rd Annual J.P. Morgan Healthcare Conference

January 14, 2025

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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

In vivo approaches **leveraging LNP delivery**

CAR T

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

CTX112™ shows promising efficacy/safety profile in oncology

Expanding CTX112 into autoimmune disease to significantly increase value

CTX131™ and **autologous anti-GPC3 in solid tumors** to further diversify platform

In Vivo

Establishing **LNP-mRNA platform**, initially beginning with liver

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

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

Building **extrahepatic** and **next-generation editing** capabilities

T1D

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

Goal to achieve **insulin independence without need for constant immunosuppressive regimens**

Developing both device (CTX211™) and deviceless (CTX213™) approaches

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 / autoimmune and regenerative medicine
- Opportunistic business development across the portfolio

2025

Sector-Leading Biotech

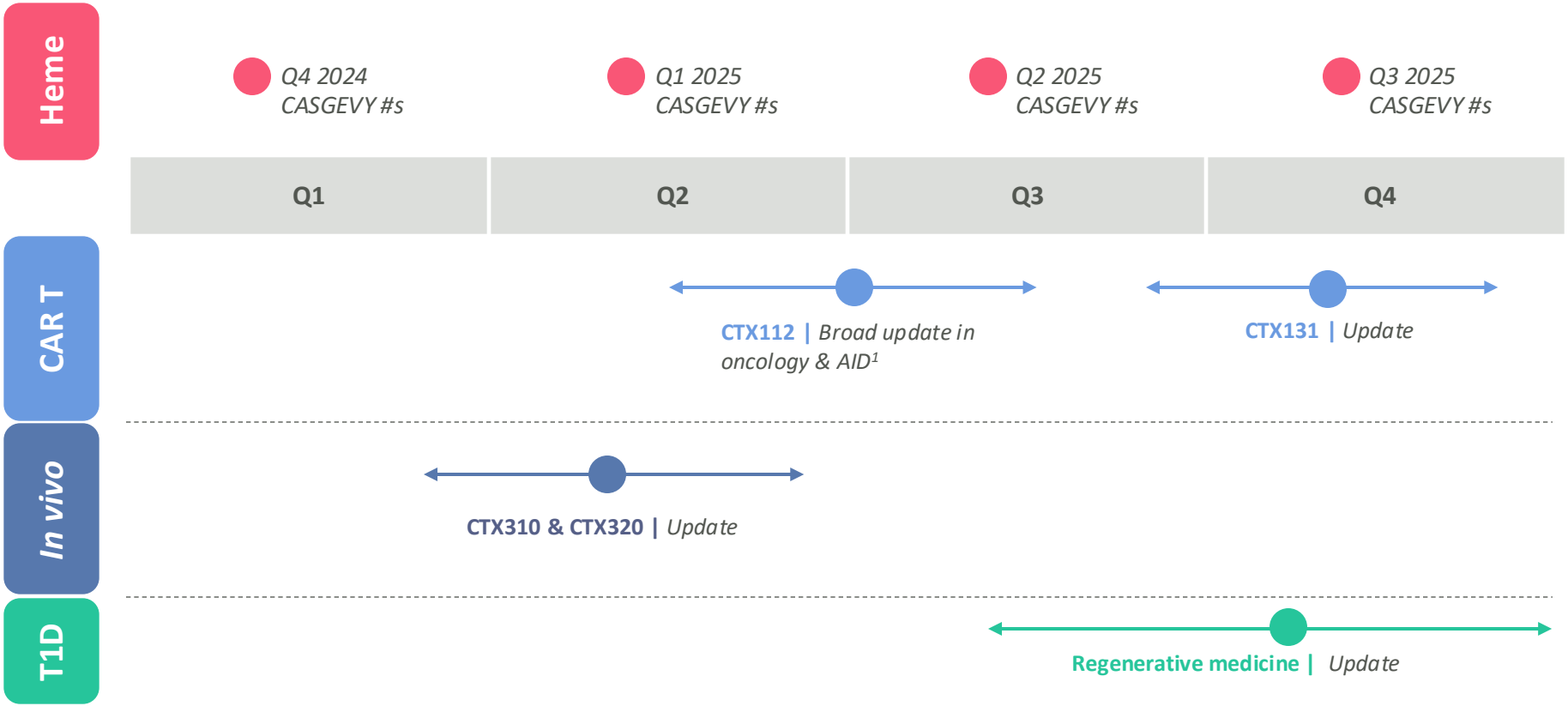
- CASGEVY revenue provides a path to a sustainable biotech company
- Clinical programs progress into later stages of development and potential approval
- Platform engine generating 1 to 2 new IND/CTAs per year
- Continued business development activities based on strategic priorities

2026+

Established efficient operating model and strong balance sheet of ~$1.9 billion[1]

[1] *Pro forma* as of 12/31/2024

Anticipated Key Milestones in 2025



[1]AID: Autoimmune Diseases

Hemoglobinopathies

2024 Was 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

TIME

Cutting Edge Gene Therapy

Vertex Pharmaceuticals and CRISPR Therapeutics Casgevy

Addressable Market[2]

~60,000

Severe patients in approved territories amenable for treatment

As of the end of 2024, CASGEVY was approved in 8 jurisdictions, >50 authorized treatment centers (ATCs) have been activated globally and >50 patients have initiated cell collection

[1] Approved by the U.S. FDA for treatment of patients aged 12 years and older with sickle cell disease (SCD) with recurrentvaso 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 isappropriate 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, Canada, Switzerland, and United Arab Emirates (UAE)

2025 is 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)

Growing into Untapped Middle East and ex-U.S. Markets

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

NHS

VISION رؤيـــة 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

Investments made to meet global demand for disease-modifying therapy

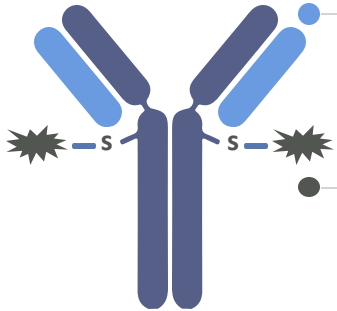
CMMI: Center for Medicare and Medicaid Innovation; GCC: Gulf Cooperation Council

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

Serial Innovation in Enabling Technologies Will Broaden Access

Targeted Conditioning

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



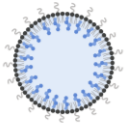
- Proprietary **GMP monoclonal antibody** with **short half-life** to enable rapid infusion of edited cells
- Validated **GMP toxin** with HSC activity and **reduced hydrophobicity** to limit non-target cell toxicity

Studies in non-human primates (NHP) ongoing

150k+ addressable patients worldwide

In Vivo Editing of HSCs

DELIVERY | EDITING

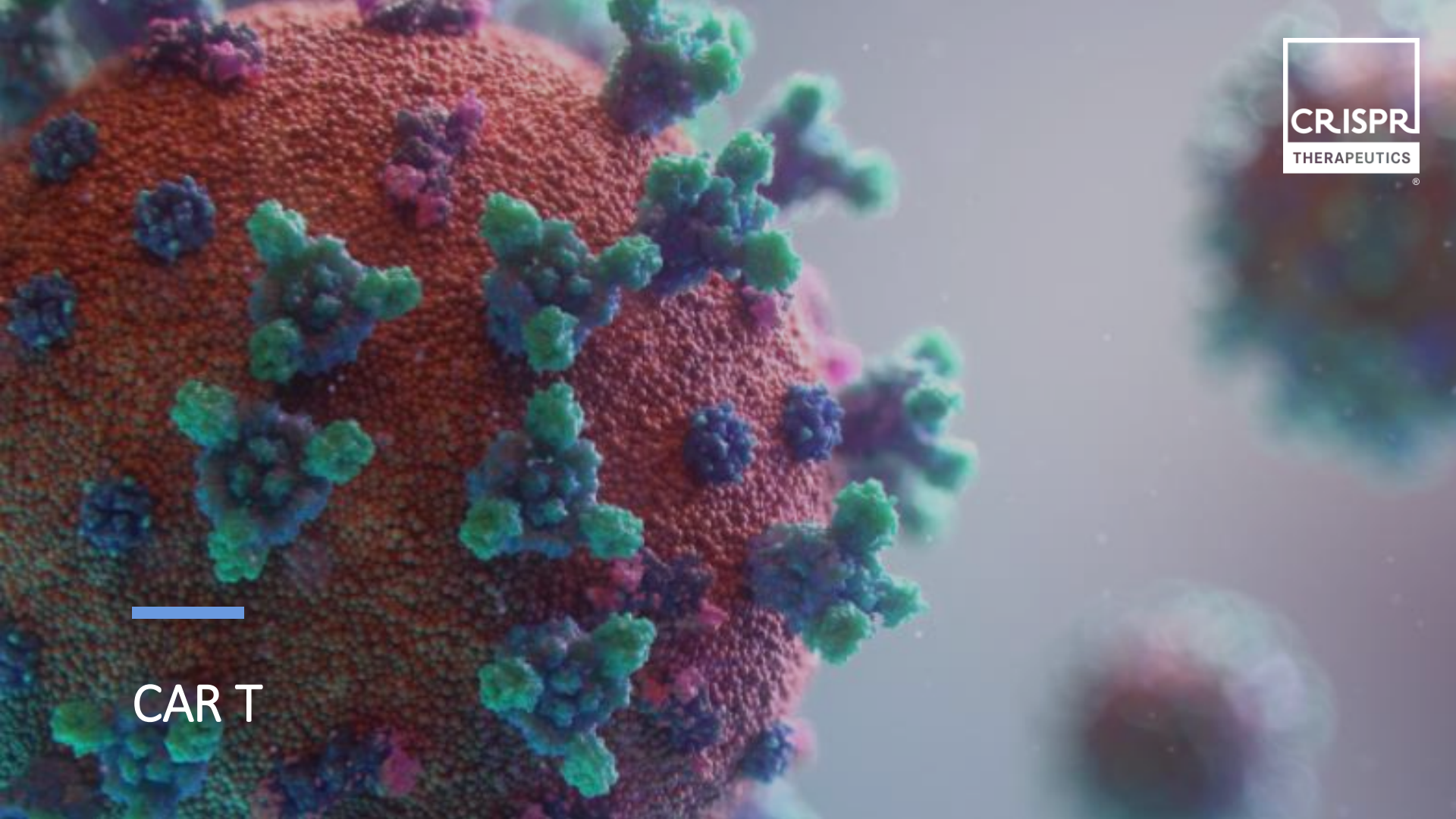


Creating optimized system for *in vivo* HSC editing with ideal characteristics, including:

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

Core research focus in 2025 – NHP studies ongoing

400k+ addressable patients worldwide



CAR T

Best-in-Class Cell Therapy Platform for the Treatment of Cancer and Autoimmune Disease

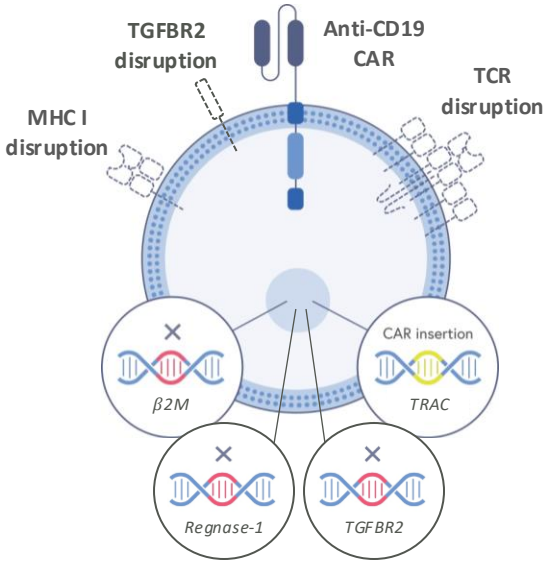
CTX112	CTX131	Autologous GPC3
Currently in Phase I/II trial in r/r NHL, plus Phase I trial in SLE/SSc/IIM	Currently in Phase I/II trial in RCC, plus Phase I/II trial in TCL	Ongoing preclinical work with anti-GPC3 autologous CAR T with TGFBR2 KO
Update mid-2025	**Update in 2025**	**IND/CTA submission in 1H 2025**

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 is 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

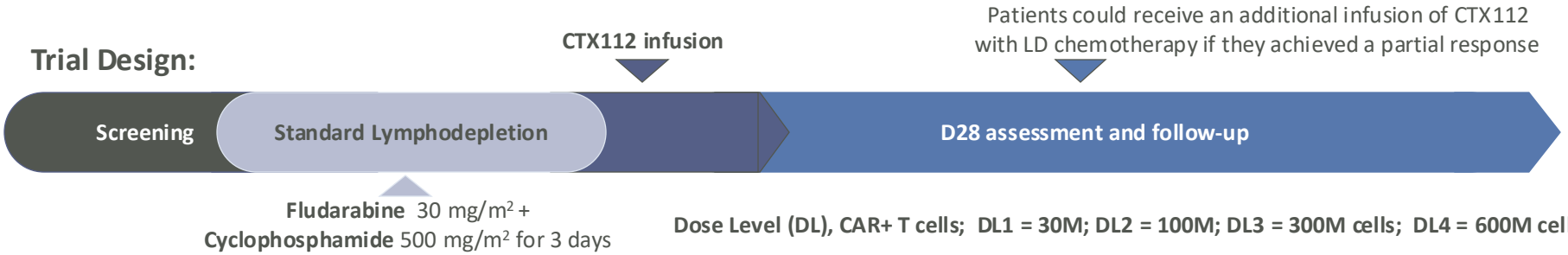
- Ability to multiplex gene edits precisely and efficiently
- Comprehensive and FDA-validated genomic analysis
- Scalability and low COGS to enable global expansion
- In-house manufacturing enables direct control over process and timelines

Multiple scientific, manufacturing and regulatory competitive advantages for CTX112

CTX112 Phase I 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

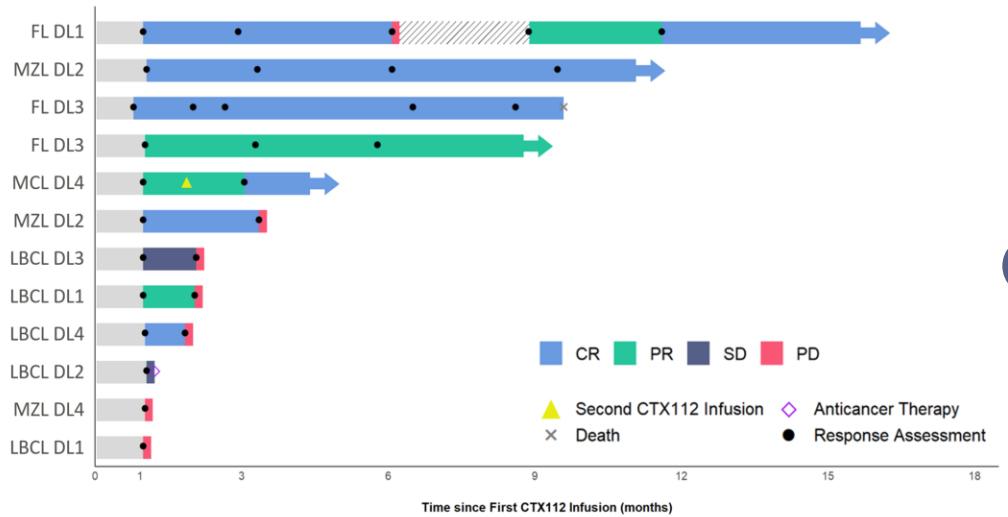
- CR rate
- Duration of response (DOR)
- Progression-free survival (PFS)
- Overall survival

(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)**

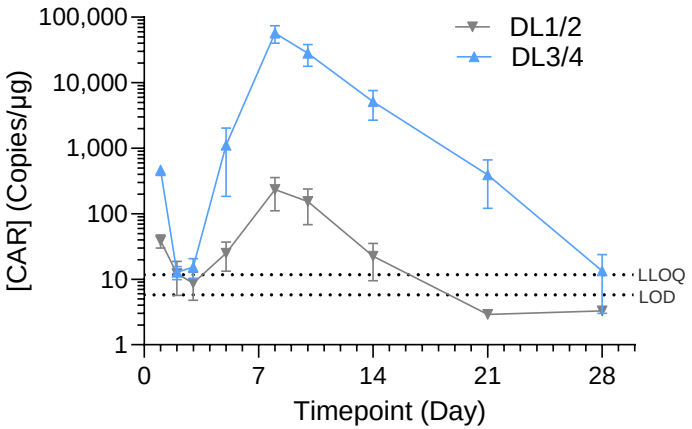
ORR/CR rate in line with approved autologous CAR T[1]

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

New 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*

New CTX112 Data Demonstrates 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 fast enrollment to dosing without the need to pause immunosuppressants • **Significantly lower COGS and scalability** are critical for expanding 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** (i.e., 100% OR rate)
CTX112 vs. Other Allogeneic CAR T / NK	• **Case studies** from other allogeneic CAR T therapies in AID **provides derisking for CTX112** • CTX112 is potentially superior with potency edits that lead to **significantly higher CAR T cell expansion and functional persistence**

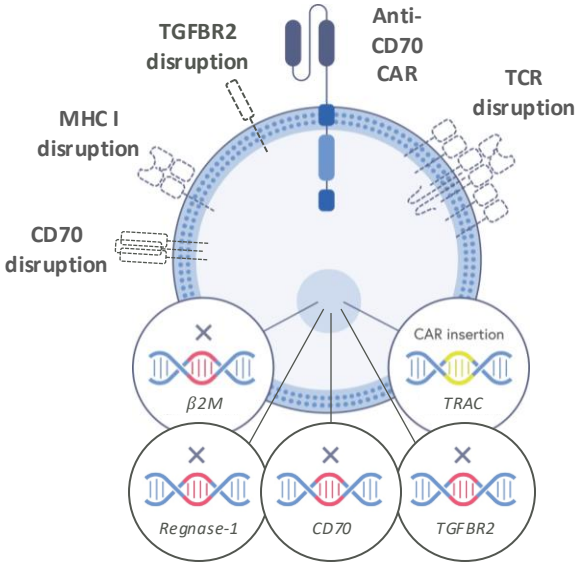
Broad CTX112 update across oncology and autoimmune disease expected in mid-2025

Next-Generation CAR T for Solid Tumors

Solid Tumor CAR T pipeline

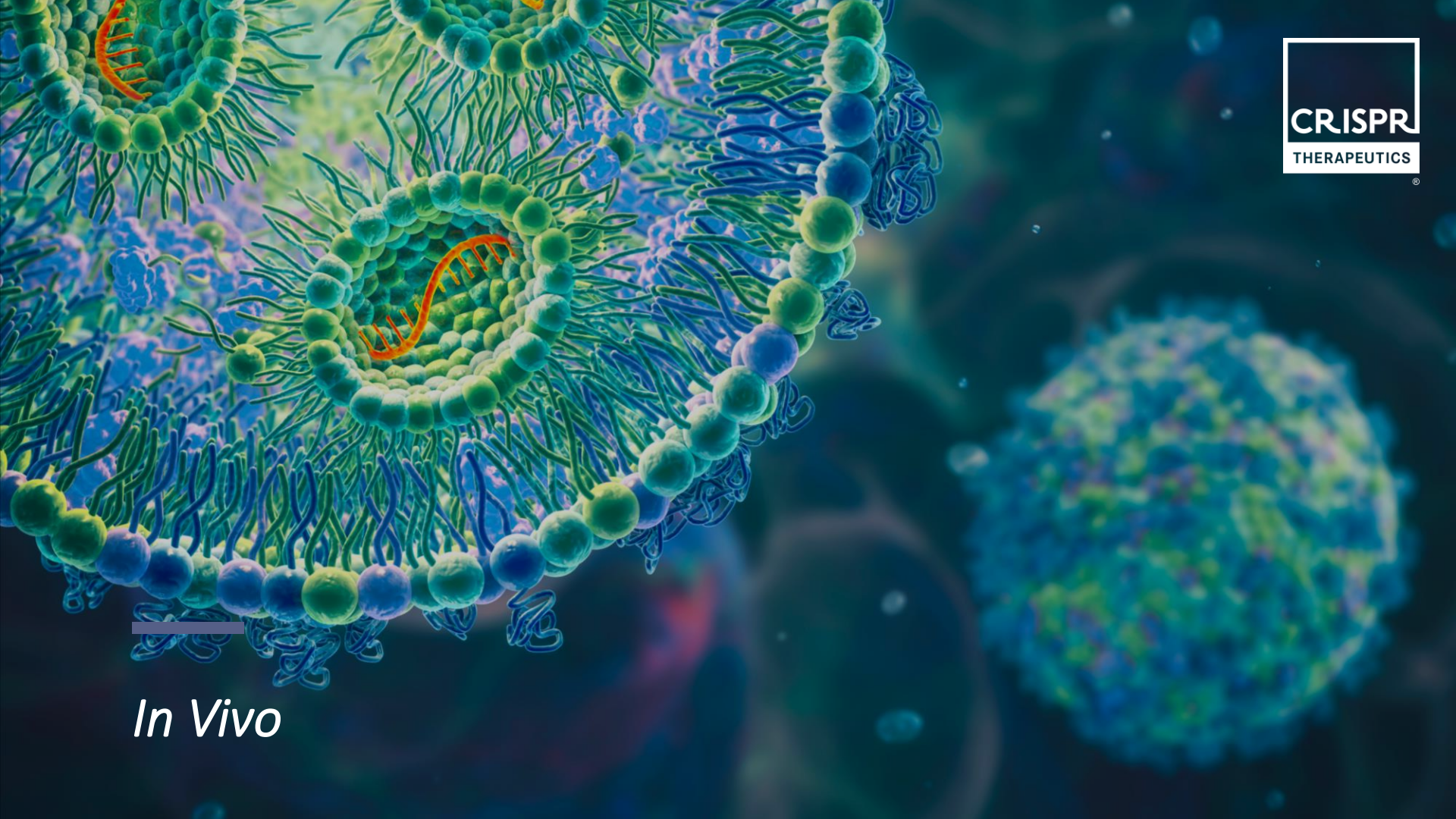
Program	Indications
CTX131 Anti-CD70 allogeneic CAR T	▪ **Phase I trial in RCC** and other solid tumors ongoing; **Phase I trial in hematologic malignancies, including T cell lymphomas (TCL)** dose escalation ongoing ▪ Update in 2025
Anti-GPC3 autologous CAR T with TGFBR2 KO	▪ **IND/CTA submission for Phase I trial in HCC** in 1H 2025 ▪ **TGFB edit prevents exhaustion**; with validating data from clinical trials in China ▪ **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

CTX320

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

Update in 1H 2025

CTX310

ANGPTL3 targeted asset with potential across multiple indications

Update in 1H 2025

CTX340™ / CTX450™

Additional preclinical programs targeting AGT and ALAS1 respectively

Progressing to IND/CTA

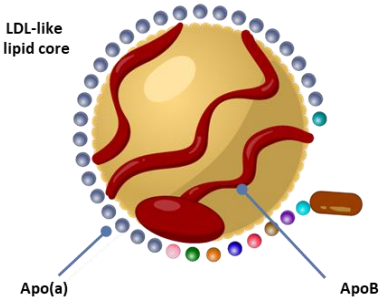
Program	Indication(s)	Research	IND-enabling	Clinical
CTX310: ANGPTL3	HeFH[1], HoFH[2], Mixed dyslipidemias, and SHTG[3]	●	●	●
CTX320: Lp(a)	ASCVD with elevated Lp(a)	●	●	●
CTX340: AGT	Refractory hypertension	●	●	○
CTX450: ALAS1	Acute hepatic porphyria	●	●	○

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

Lp(a) is Emerging as a Key Target to Potentially Reduce CV Events

Lp(a): An independent risk factor of atherosclerotic cardiovascular disease (ASCVD)

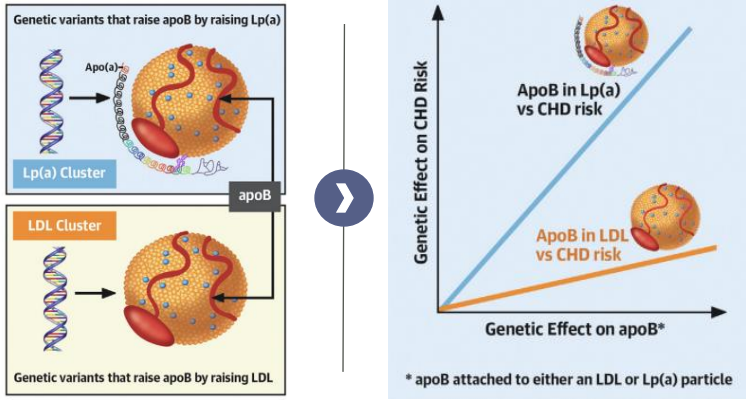
Lp(a) contains a single apo(a) molecule covalently bound by a disulfide bridge to ApoB



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 of elevated Lp(a) is cumulative throughout a person's lifetime and cannot be sufficiently reduced by lifestyle changes or currently approved therapies

Comparison of atherogenicity of Lp(a) and LDL

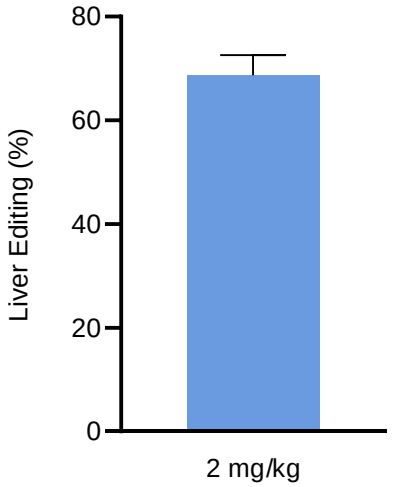


Lp(a) is 6x more atherogenic than LDL on a per-particle basis[4], highlighting its significance as a critical target for drug-based interventions

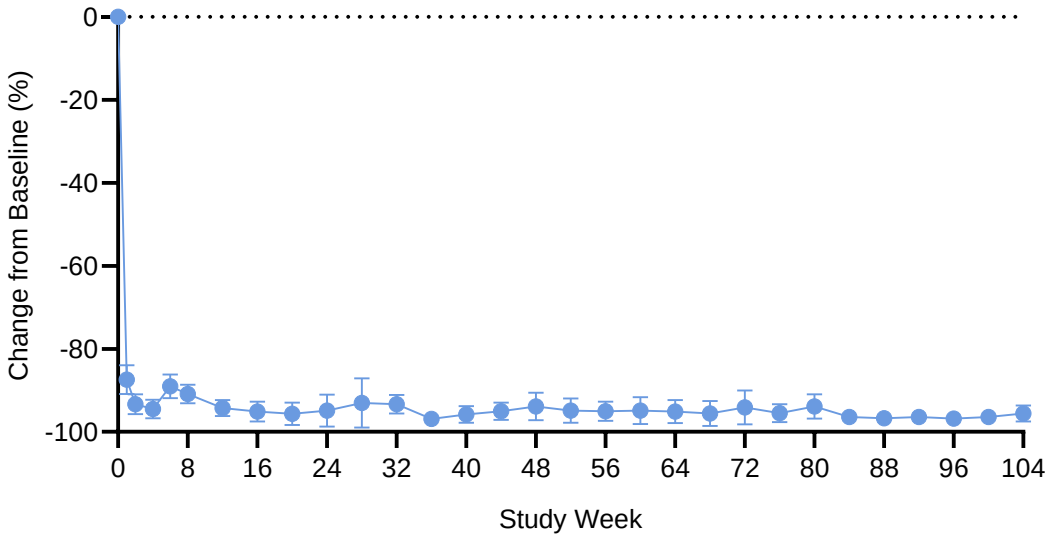
Lp(a): lipoprotein(a); [1] Enas et al. 2019; [2] Gurdasani et al. 2012; [3] Laschkolnig et al. 2014; [4] Björnson et al. 2024

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 shows 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) and CVD
- Adequate renal, liver, cardiac, and pulmonary organ function
- No significant co-morbidities

Endpoints

- Incidence of adverse events, defined as DLTs
- Change in Lp(a) compared to baseline
- Pharmacokinetics

Phase II

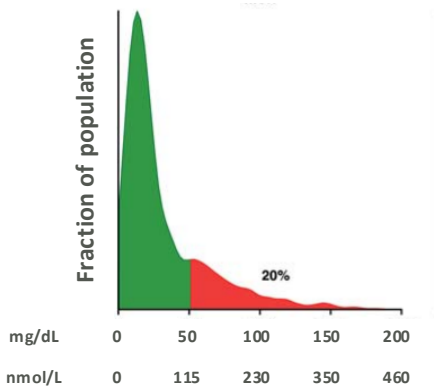
- Patients with elevated levels of Lp(a)
- Phase II dose informed by Phase I

CTX320 update in 1H 2025

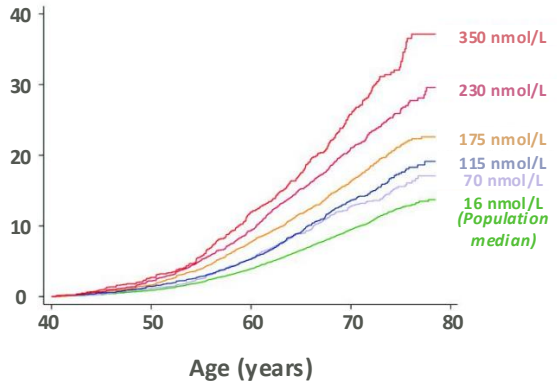
CTX320 Has Potential to Address Population with Elevated Lp(a)

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 has potential to significantly de-risk Lp(a)

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

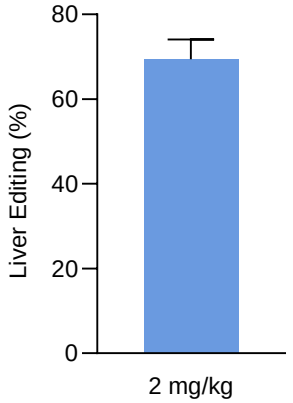
CTX310 Targeting ANGPTL3 for Cardiovascular Disease

Natural loss-of-function mutations in *ANGPTL3* are associated with reduced LDL-C, triglycerides (TG), and ASCVD risk without any negative impact on overall health[1,2]

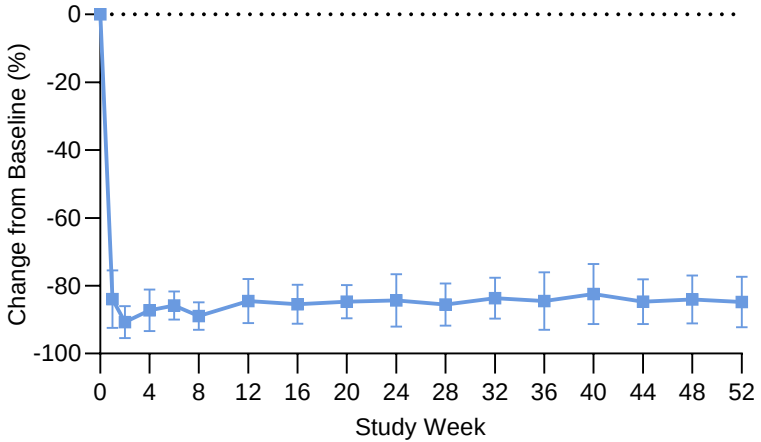
Phase I trial in HoFH, sHTG and Mixed dyslipidemias; >10M addressable U.S. patients

A single dose of CTX310 durably reduced ANGPTL3 and triglycerides in NHPs out to 1 year

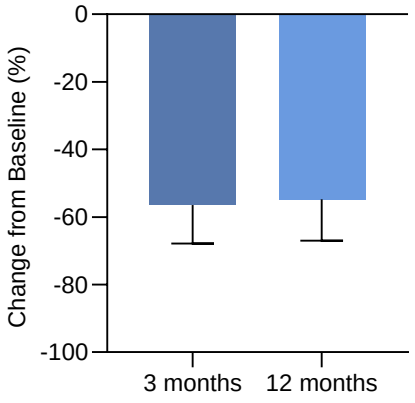
~70% editing of *ANGPTL3*



Sustained reduction in plasma ANGPTL3 in NHPs



Sustained reduction in TG



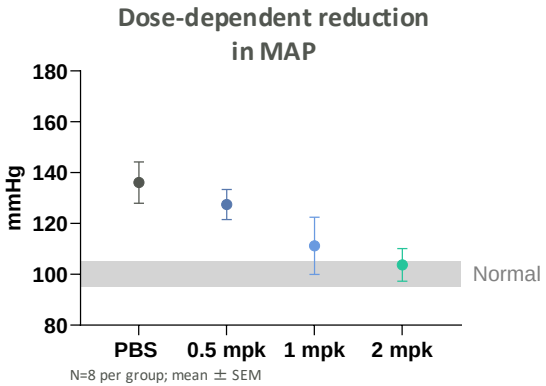
CTX310 update in 1H 2025

Single dose of CTX310 (2 mg/kg) administered to non-human primates (NHPs) (N=8) on Day 1; study ongoing; Editing rate reflects whole liver editing; HoFH; Homozygous familial hypercholesterolemia; sHTG; Severe hypertriglyceridemia [1] Minicocci et al. 2012; [2] D'Erasmo et al. 2023

Two Additional Programs Advancing Toward Clinic

CTX340 Targeting AGT For Refractory Hypertension

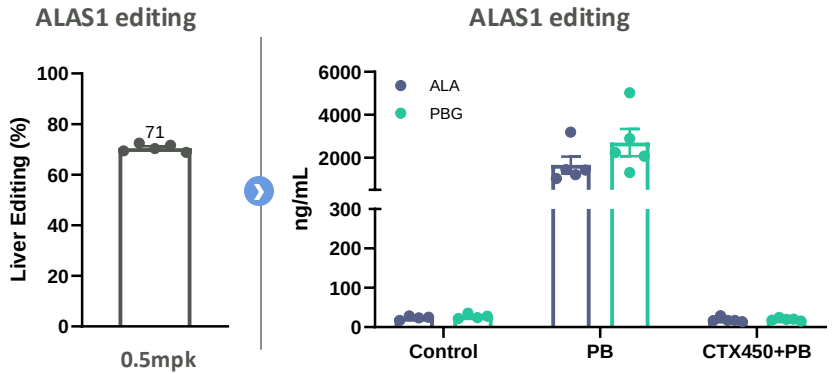
- Hypertension is the leading cause of cardiovascular morbidity and mortality worldwide[1,2]
- By going upstream of typical therapeutic approaches by targeting AGT, we can significantly impact hypertension and reduce dependence on other antihypertensives



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

2025 Could be a Year of Significant Value Creation

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

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

- Quarterly updates for CASGEVY launch progress
- CTX310 and CTX320 update in cardiovascular indications in the first half of 2025
- CTX112 update in oncology and autoimmune disease in mid-2025
- Additional updates across our pipeline including CTX131 and T1D in 2025

Strong balance sheet with clear path to a sustainable biotechnology company

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

