CRISPR Therapeutics

Creating transformative gene-based medicines for serious diseases

Corporate Overview

August 2018

Forward-Looking Statements

This presentation and other related materials contain forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, but not limited to, statements concerning: the timing of filing of clinical trial applications and INDs, any approvals thereof and timing of commencement of clinical trials, the timing, therapeutic value, development, and commercial potential of CRISPR/Cas9 gene editing technologies and therapies, the sufficiency of CRISPR's cash resources and the intellectual property coverage and positions of CRISPR, its licensors and third parties. All statements, other than statements of historical facts, included or incorporated by reference in this presentation and other related materials, including statements regarding CRISPR's strategy, future operations, future financial position, future revenue, projected costs, prospects, plans, and objectives of management, are forward-looking statements. The words "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "target," "should," "would," and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. CRISPR may not actually achieve the plans, intentions, or expectations disclosed in these forward-looking statements, and you should not place undue reliance on these forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in these forward-looking statements as a result of various factors, including: uncertainties regarding the intellectual property protection for CRISPR's technology and intellectual property belonging to third parties; uncertainties inherent in the initiation and completion of preclinical studies for CRISPR's product candidates; availability and timing of results from preclinical studies; whether results from a preclinical trial will be predictive of future results of the future trials; expectations for regulatory approvals to conduct trials or to market products; and those risks and uncertainties described under the heading "Risk Factors" in CRISPR's most recent annual report on Form 10-K, and in other filings that CRISPR has made or may make with the U.S. Securities and Exchange Commission.

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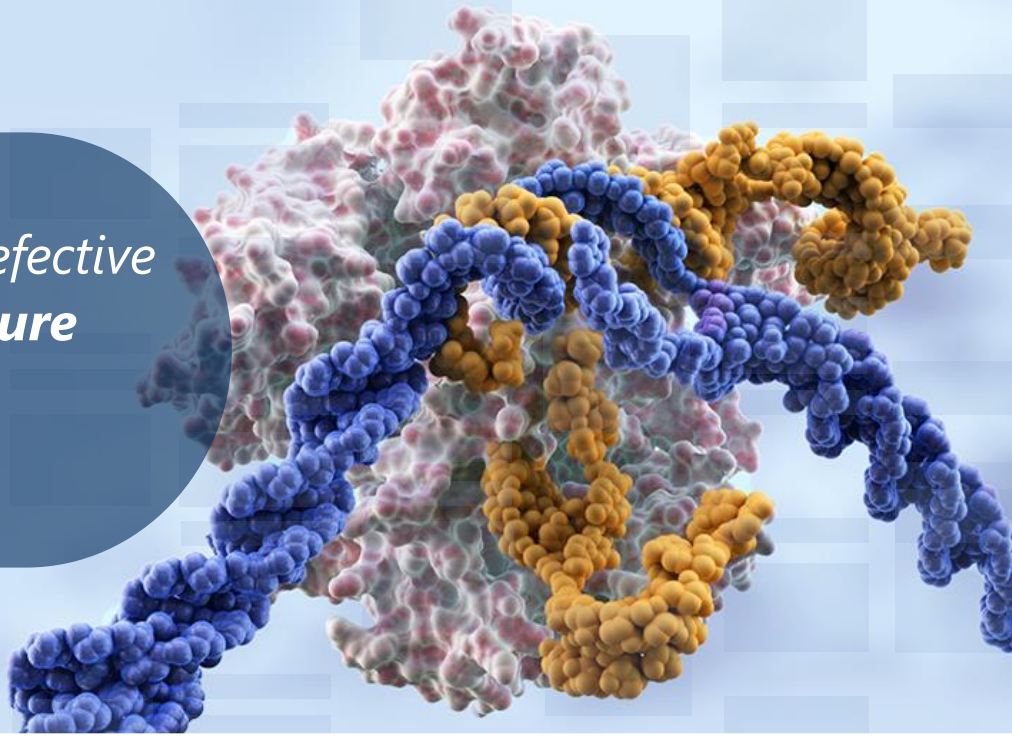
The CRISPR/Cas9 Revolution

> *A new technology for 'editing' defective genes has raised hopes for a* ***future generation of medicines***

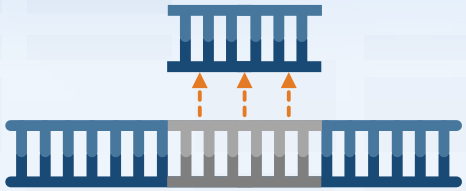
THE WALL STREET JOURNAL.



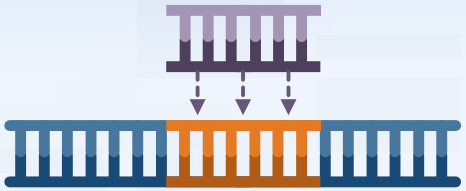
Specific, efficient, and versatile platform

DISRUPTION

DELETION



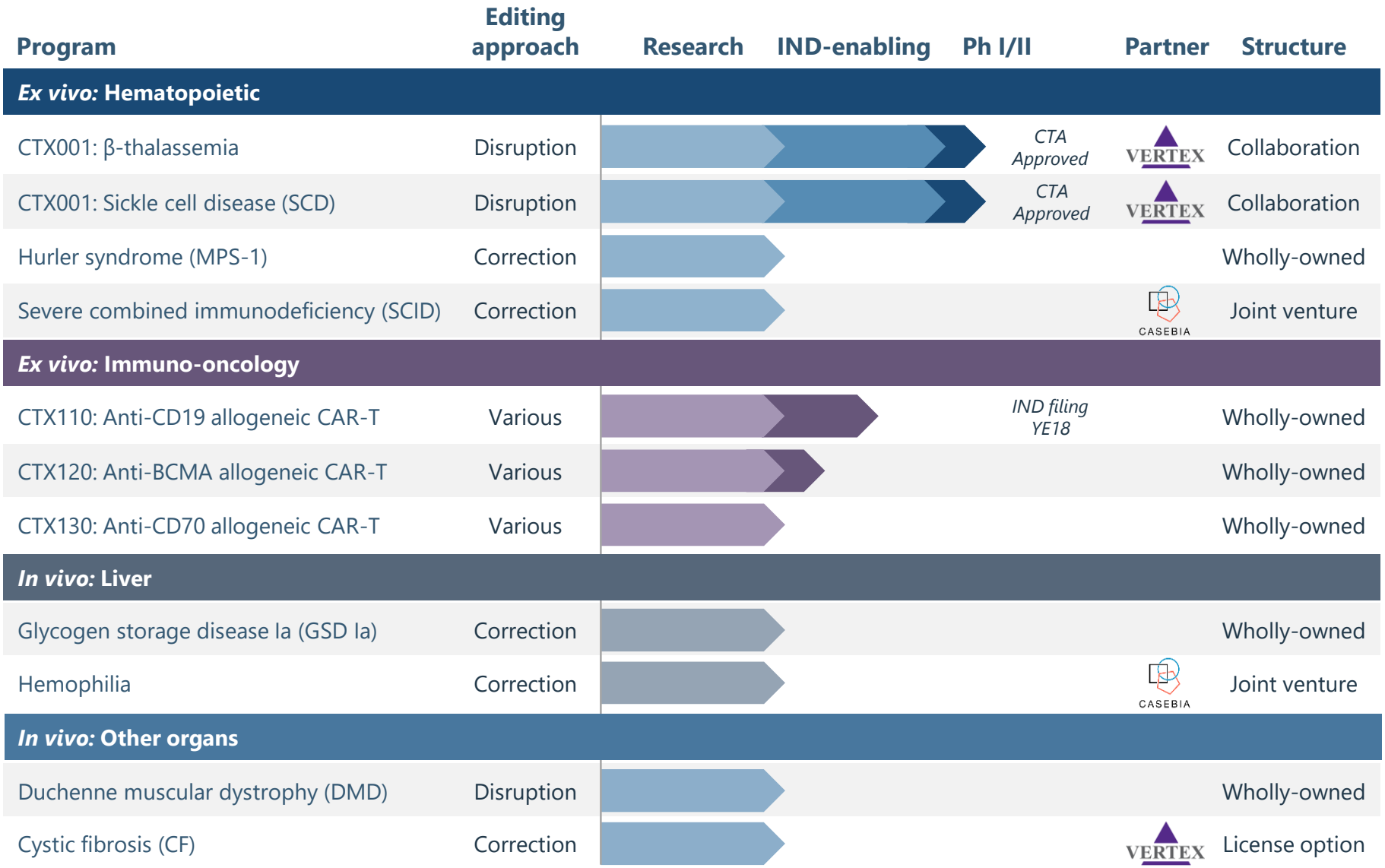
CORRECTION



CRISPR Therapeutics Highlights

LEADING GENE-EDITING COMPANY	Rapidly translating revolutionary CRISPR/Cas9 technology into transformative therapies
PIONEERING CRISPR IN THE CLINIC	Filed first company-sponsored CTA for a CRISPR-based therapeutic; CTX001 on track to initiate trials in 2018 in hemoglobinopathies
NEXT-GENERATION I/O PLATFORM	Advancing wholly owned, potentially best-in-class gene-edited allogeneic CAR-T products toward the clinic
ADVANCING *IN VIVO* APPLICATIONS	Pursuing select *in vivo* indications enabled by in-licensed technologies, platform improvement, and strategic partners
UNIQUE CASEBIA JOINT VENTURE	50% ownership of Casebia broadens our pipeline and supports our platform improvement efforts; funded by ~$265M from Bayer
STRONG IP & FINANCIAL POSITION	Strong IP and robust financial position: $341.8 million in cash as of 3/31/18

Our Portfolio



Program	Editing approach	Research / IND-enabling / Ph I/II	Partner	Structure
***Ex vivo:* Hematopoietic**				
CTX001: β-thalassemia	Disruption	*CTA Approved*	VERTEX	Collaboration
CTX001: Sickle cell disease (SCD)	Disruption	*CTA Approved*	VERTEX	Collaboration
Hurler syndrome (MPS-1)	Correction			Wholly-owned
Severe combined immunodeficiency (SCID)	Correction		CASEBIA	Joint venture
***Ex vivo:* Immuno-oncology**				
CTX110: Anti-CD19 allogeneic CAR-T	Various	*IND filing YE18*		Wholly-owned
CTX120: Anti-BCMA allogeneic CAR-T	Various			Wholly-owned
CTX130: Anti-CD70 allogeneic CAR-T	Various			Wholly-owned
***In vivo:* Liver**				
Glycogen storage disease Ia (GSD Ia)	Correction			Wholly-owned
Hemophilia	Correction		CASEBIA	Joint venture
***In vivo:* Other organs**				
Duchenne muscular dystrophy (DMD)	Disruption			Wholly-owned
Cystic fibrosis (CF)	Correction		VERTEX	License option

Our Therapeutic Programs

Hemoglobinopathies
Ex vivo *lead candidate in genetically-defined disease*

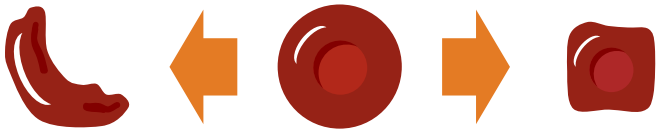
Immuno-oncology
Expand cell therapy platform with allo CAR-T pipeline

In vivo
Enable in vivo *applications through platform advancements*

Hemoglobinopathies – Devastating Blood Diseases

SICKLE CELL DISEASE (SCD) AND β-THALASSEMIA

Blood disorders caused by *mutations* in the β-globin gene



Sickle Cell | Normal Cell | **β-thalassemia**

Significant worldwide burden

300,000

60,000

Annual births in SCD and β-thalassemia, respectively

High morbidity and mortality

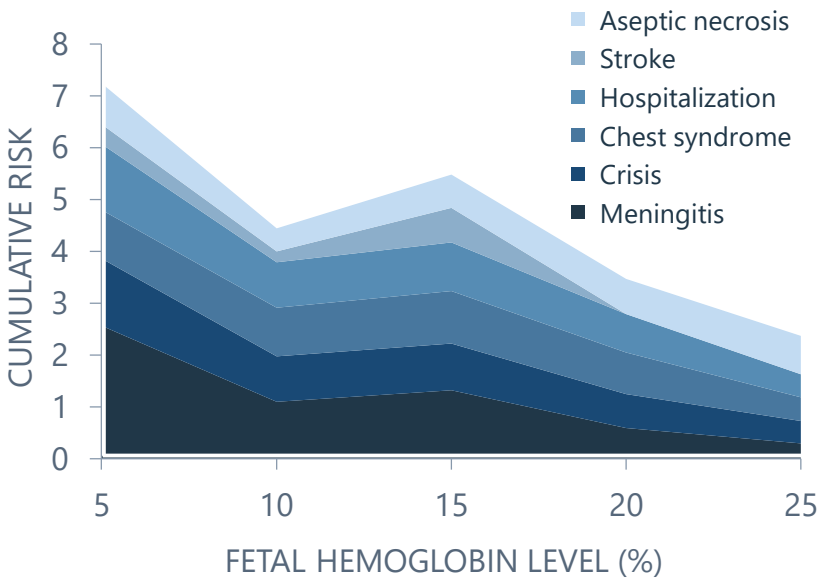
Anemia | Pain | **Early death**

Heavy burden of patient care

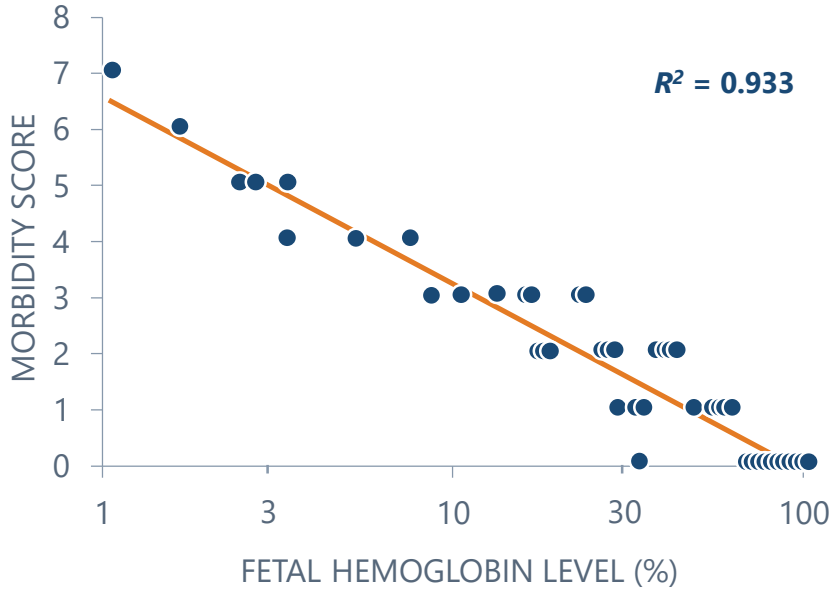
Frequent transfusions & hospitalizations

Our Approach – Upregulating Fetal Hemoglobin

REDUCED RISK OF EVENTS IN SICKLE CELL DISEASE[1]



REDUCED SYMPTOMS IN β-THALASSEMIA[2]

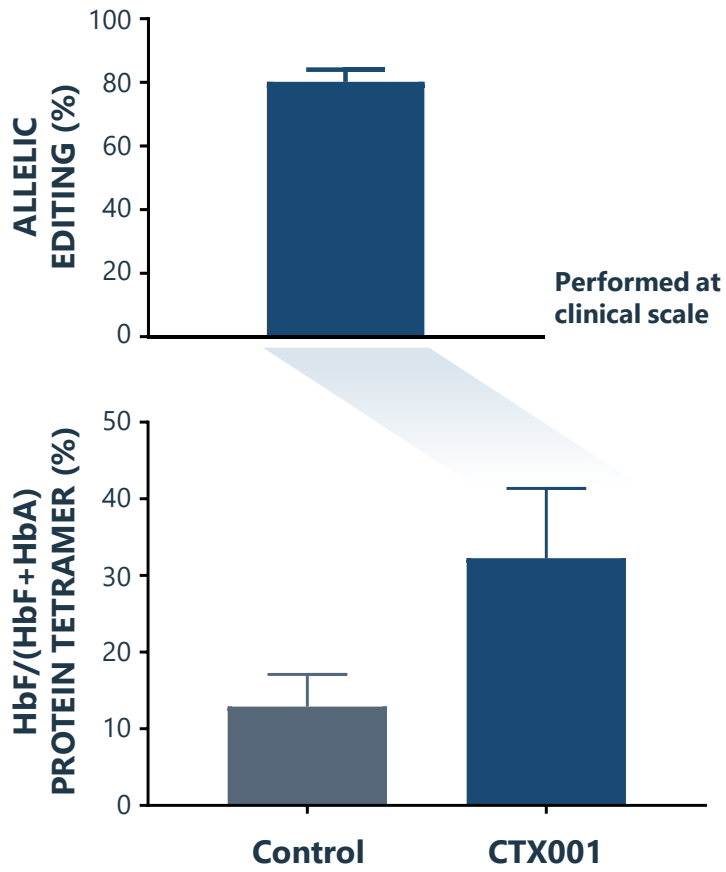


- **Naturally occurring genetic variants** cause **hereditary persistence of fetal hemoglobin** (HPFH), and **lead to reduced symptoms** in patients with sickle cell disease and β-thalassemia
- Our gene editing strategy aims to **recreate these variants** in symptomatic patients — an approach **supported by well-understood genetics**

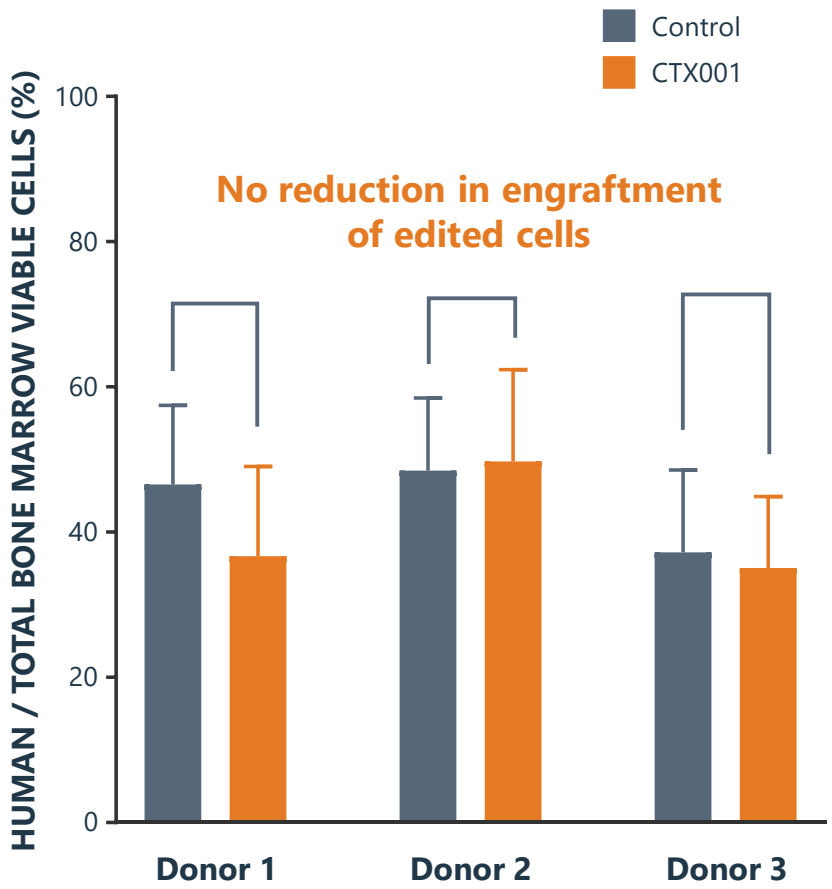
1. Powars, *et al*. Blood 1984; 2. Musallam, *et al*. Blood 2012

CTX001 Upregulates Fetal Hemoglobin and Engrafts in Mice

HIGH EDITING RATES LEAD TO ROBUST HbF INDUCTION[1]

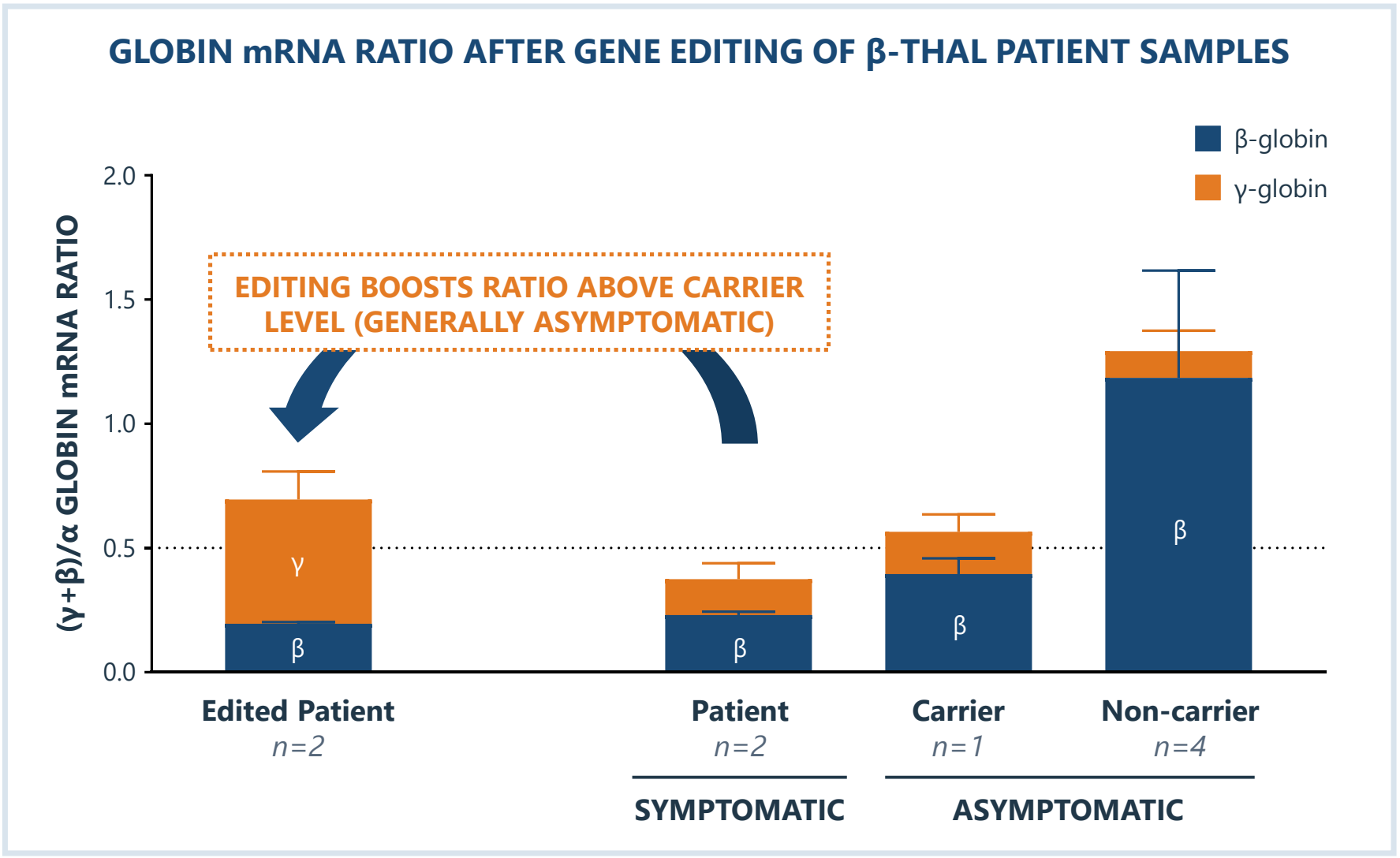


CTX001 ENGRAFTS *IN VIVO* IN MICE[2]

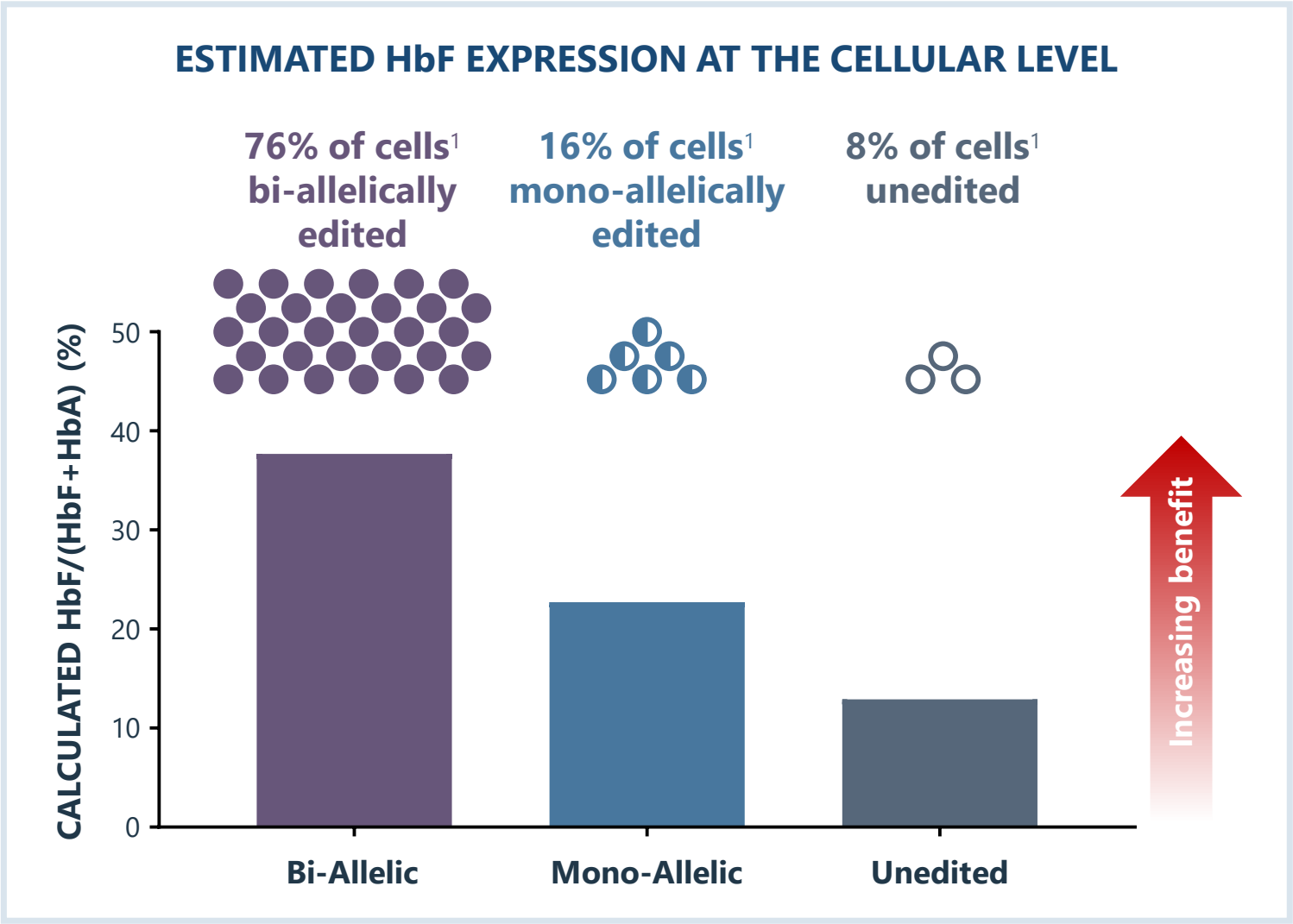


1. n=6 healthy donors; 2. 16-week engraftment data

β-thal: Editing Increases Globin Expression to Carrier Levels



SCD: Bi-Allelic Editing Leads to High HbF Protein Levels



1. n=163 single erythroid colonies derived from edited CD34+ cells from healthy donors

Pioneering CRISPR Clinical Trials

CTX001-111 and CTX001-121

Single-arm Phase 1/2 studies to assess the safety and efficacy of CTX001 in patients with β-thalassemia and SCD

Patients

Up to 45 adult patients each for transfusion-dependent β-thal and severe SCD

Sites

Sites with extensive transplant experience in countries with significant disease burden

Endpoints

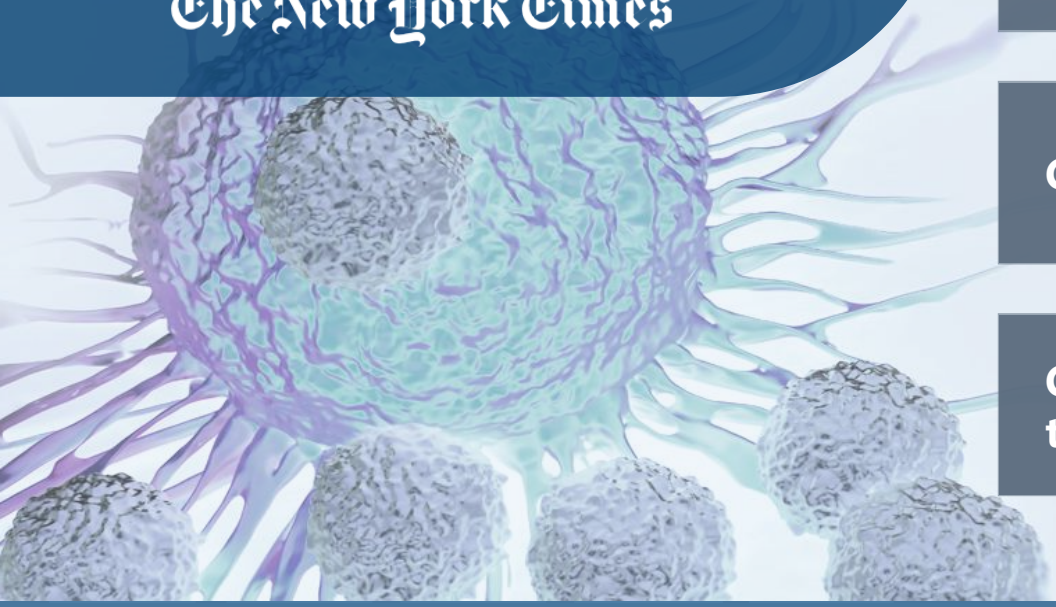
HbF levels and transfusion requirements are clinically relevant and easily measurable

Potential to expand into registrational trials, as well as to additional age cohorts and β-thal genotypes, if supported by safety and efficacy

Autologous CAR-T is Transformative, but has Limitations

CAR-T has generated **tremendous excitement . . .**

> *The first-ever treatment that genetically alters a patient's own cells to fight cancer, a milestone that is **expected to transform treatment in the coming years***
>
> The New York Times

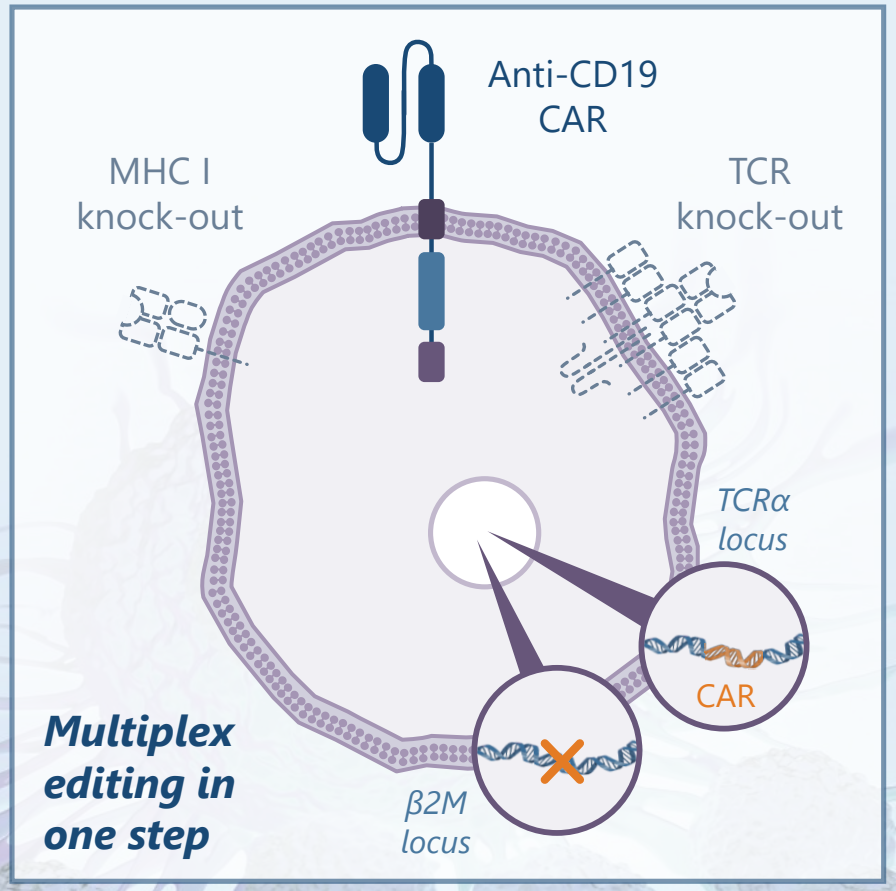


. . . But there are still **significant limitations** to autologous CAR-T

- **Patients progress or die while waiting**
- **Patient-to-patient variability**
- **Costly, complicated manufacturing**
- **Commercial challenges of bespoke therapy**

Our Approach: Gene-Edited Allogeneic CD19 CAR-T

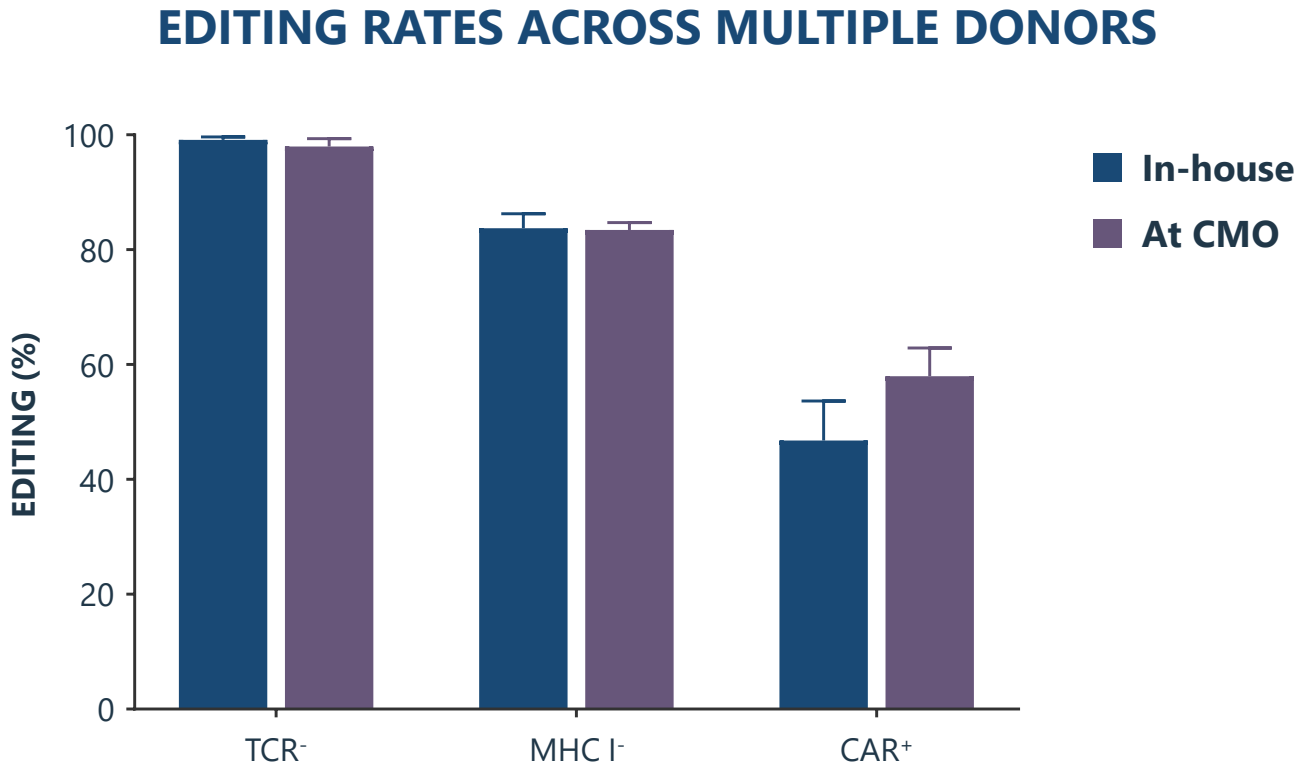
CTX110 – our initial immuno-oncology product candidate



CRISPR enables an allogeneic approach that **remedies issues with autologous CAR-T**

- **Product available immediately**
- **Consistent healthy-donor lymphocytes**
- **Low COGs and simpler manufacturing**
- **Off-the-shelf product – broader access**

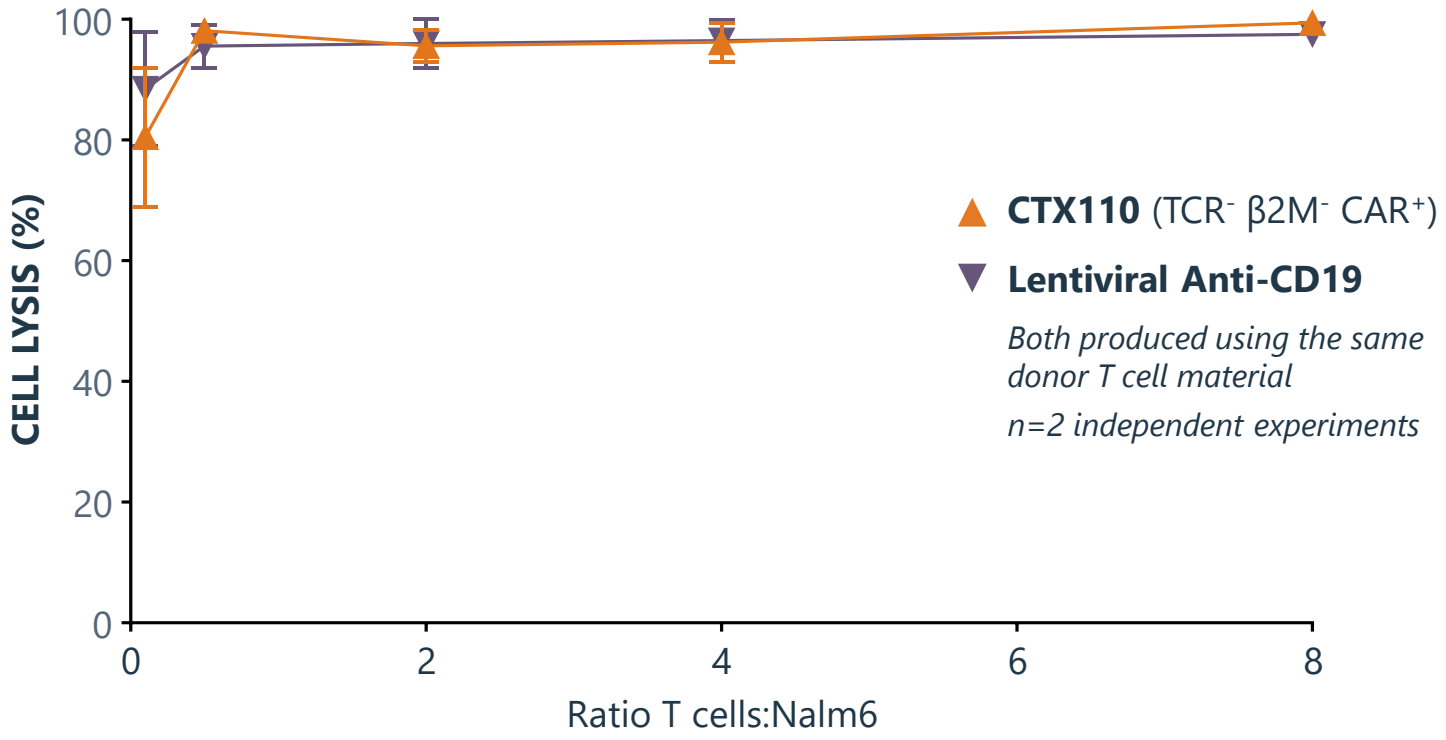
Equal or Better Editing Rates Achieved After Tech Transfer



Process development and manufacturing initiated for CTX110 – IND-enabling studies underway

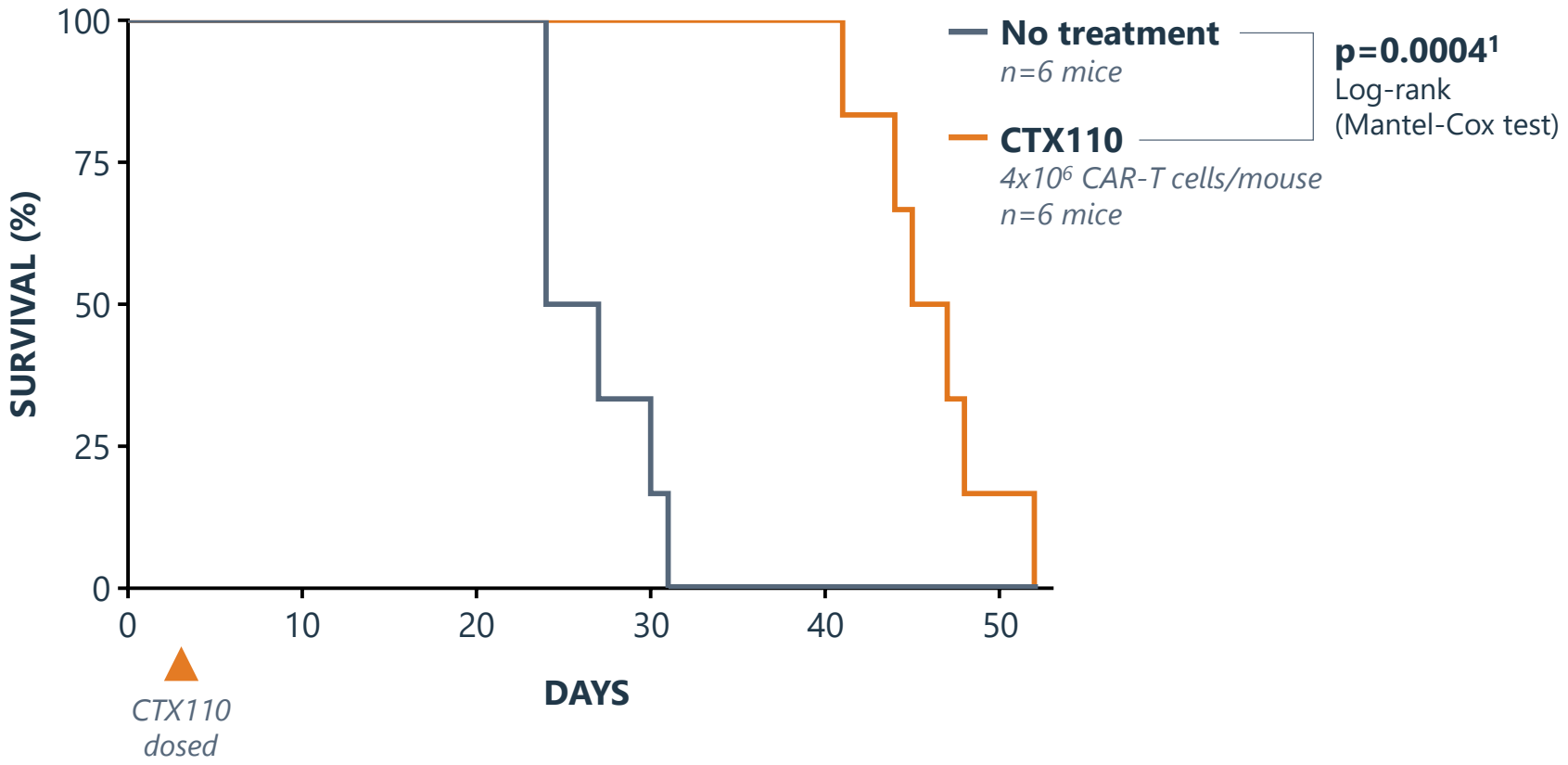
CTX110 Eliminates CD19-Expressing Tumor Cells *In Vitro*

CTX110 COMPARES FAVORABLY TO LENTIVIRAL "AUTOLOGOUS" CAR-T



CTX110 Prolongs Survival in a CD19^{+} Tumor Model *In Vivo*

PROLONGED SURVIVAL IN DISSEMINATED NALM6 B-ALL MODEL



Numerous Opportunities Beyond CTX110

Make rapid entry using validated tumor targets

Healthy-donor allo approach in well-validated tumor targets

CD19, BCMA

Expand into solid with novel targets and advanced editing

Precise edits to make CAR-T effective in solid tumors

CD70, resistance to tumor microenvironment

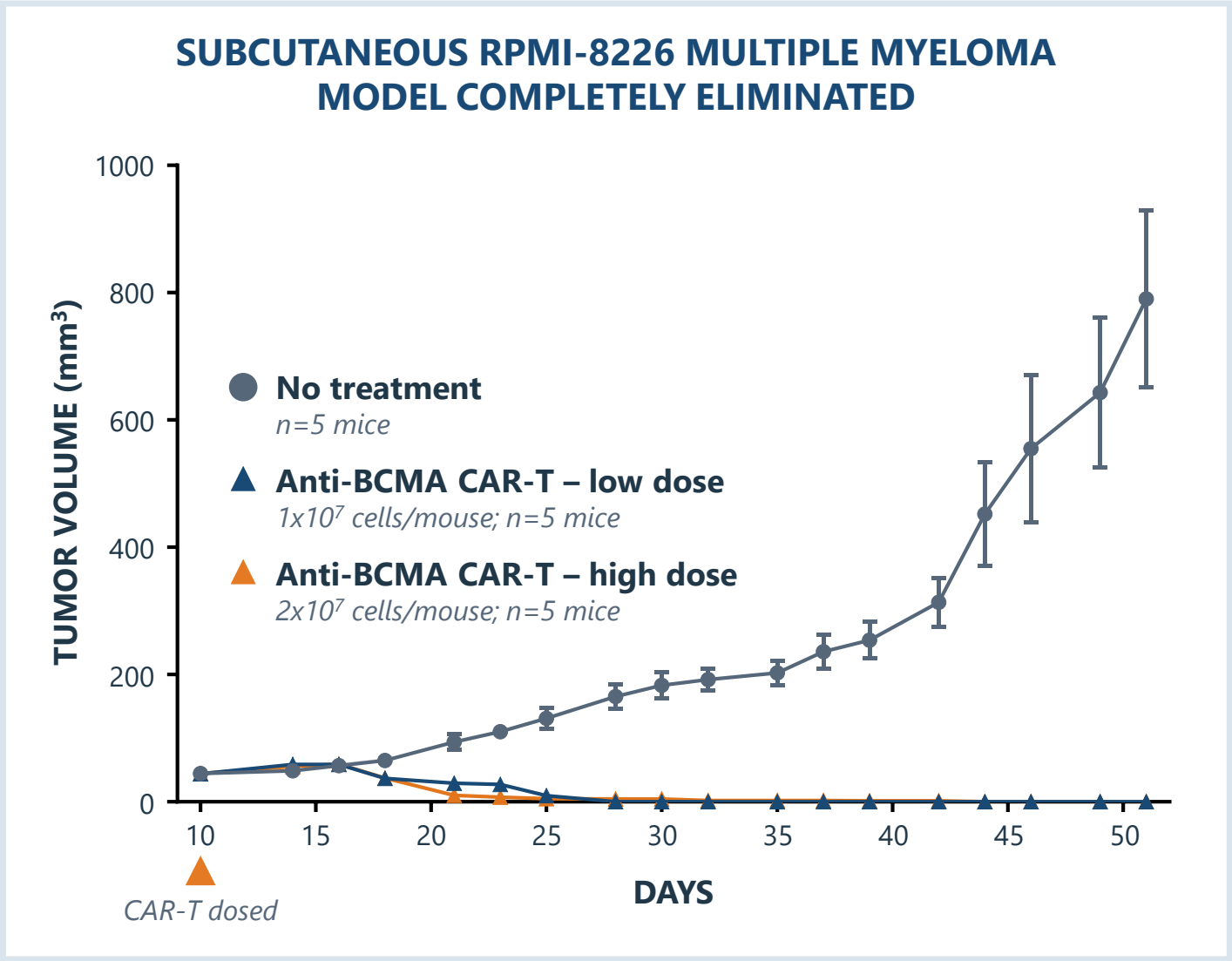
Unlock the full potential of CRISPR

Multiplex editing to enable more complex products

Switches, neoantigens, bispecifics

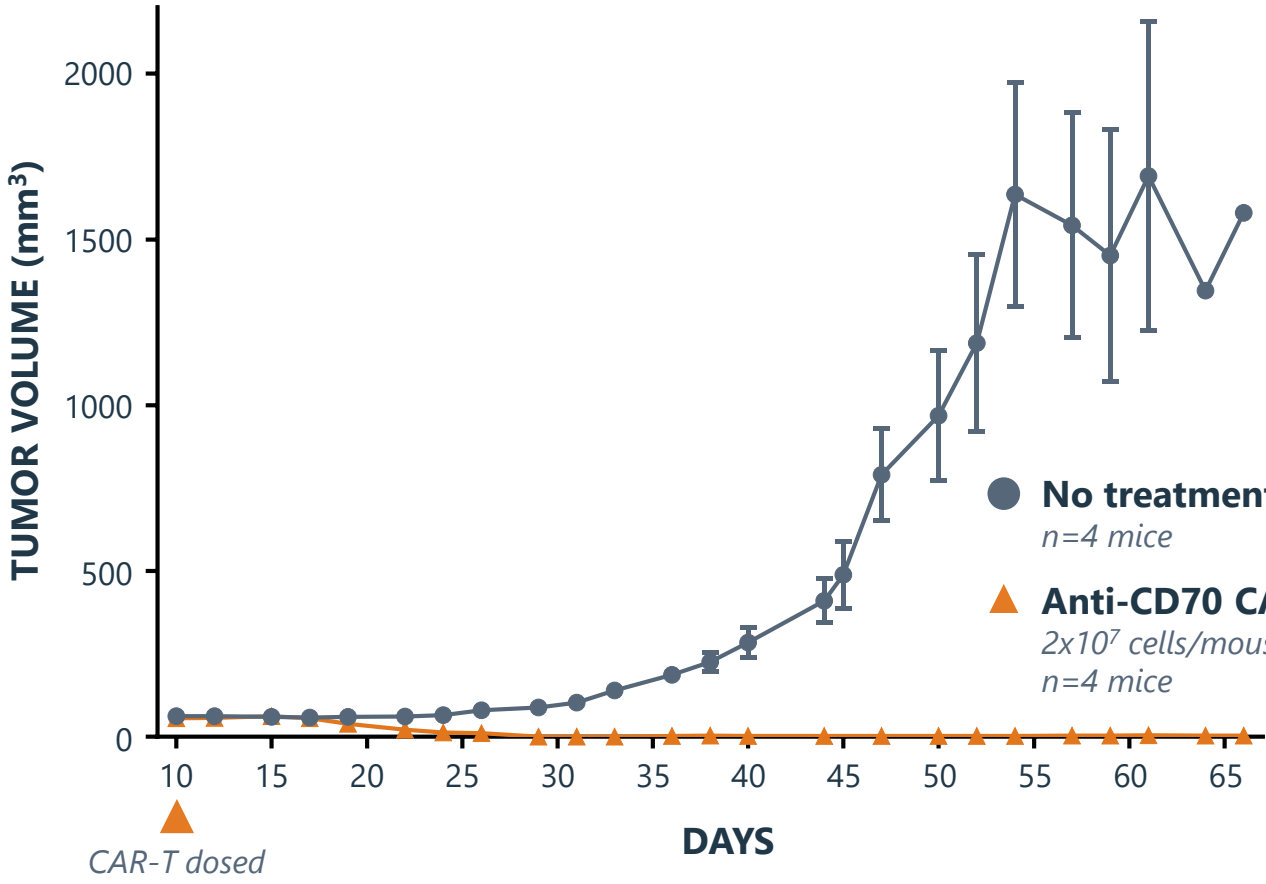
Collaborations with Neon and MGH to identify and exploit new targets

Gene-Edited Allo CAR-T Targeting BCMA



Gene-Edited Allo CAR-T Targeting CD70

SUBCUTANEOUS A498 RENAL CELL CARCINOMA MODEL COMPLETELY ELIMINATED



- **>85% CAR⁺** using a proprietary single chain made in-house
- **>99% TCR knock-out** even before purification

Delivering CRISPR/Cas9 to Unlock *In Vivo* Applications

CRISPR THERAPEUTICS

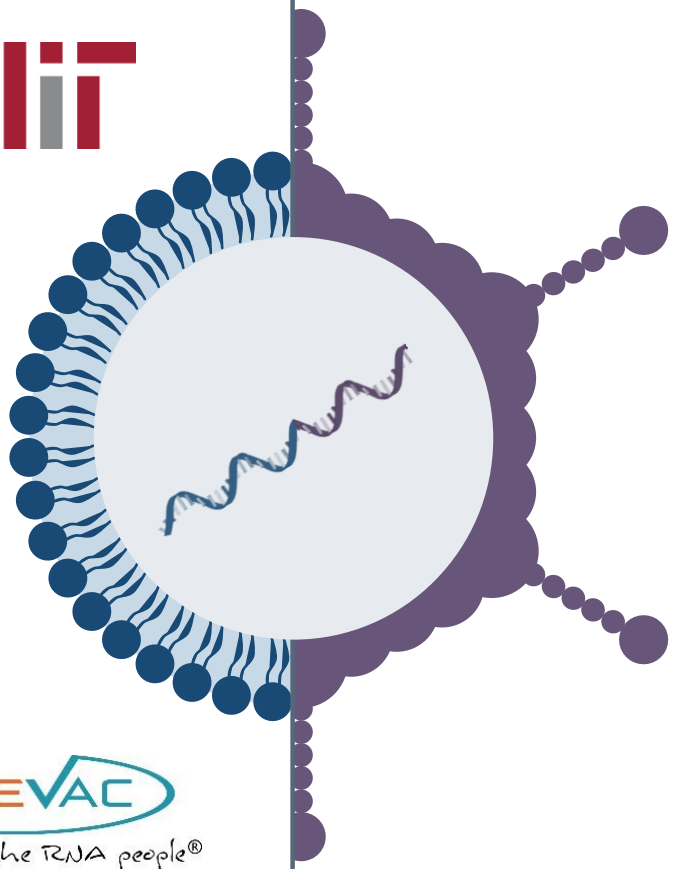
NON-VIRAL

Lipid Nanoparticles (LNPs)

- Increased potency
- Expansion beyond liver delivery
- Improved tolerability

Messenger RNA (mRNA)

- Controlled duration of expression
- Tissue specificity
- Increased potency



VIRAL

Adeno-Associated Virus (AAV)

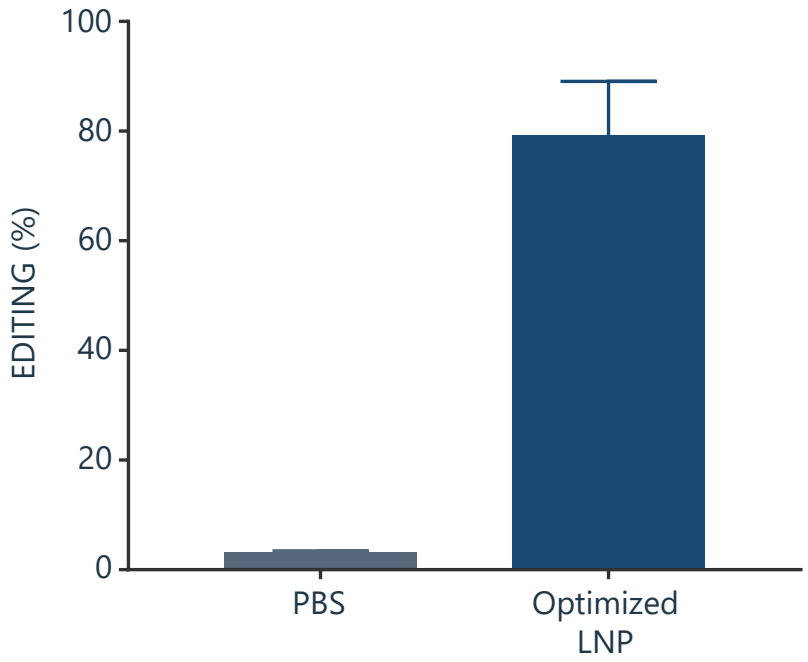
- Improved tissue specificity
- Reduced immunogenicity
- Self-inactivation

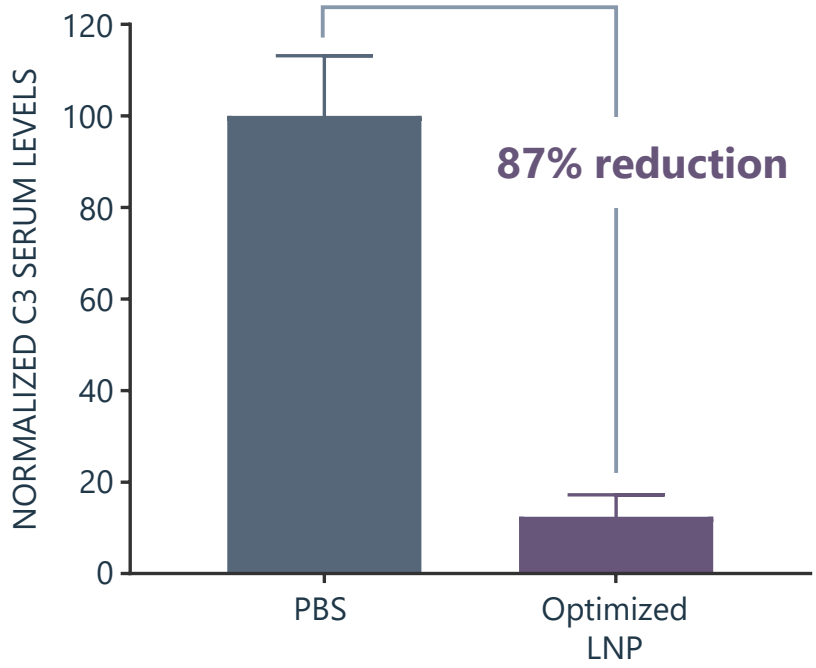
stridebio

Potent Liver Editing Using Proprietary LNP Technology

SIGNIFICANT DECREASE IN SERUM C3 LEVELS AFTER EDITING *IN VIVO*

Editing and serum protein quantified in five mice following intravenous LNP dose





~80% editing in mouse livers and 87% reduction in serum C3 protein using just 1 mg/kg total RNA

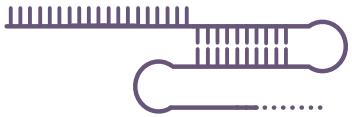
Optimizing the CRISPR/Cas9 Platform

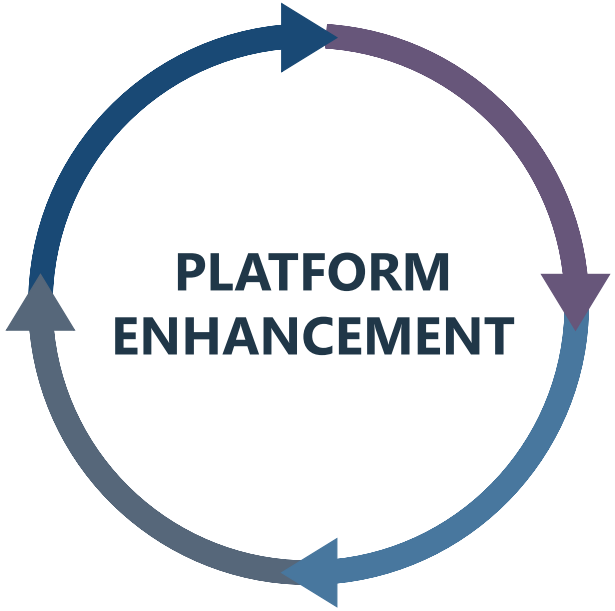
NUCLEASE ENGINEERING

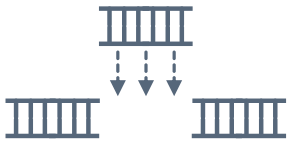
Enhance CRISPR/Cas9 system through protein engineering

GUIDE RNA OPTIMIZATION

Identify optimal guide RNA formats and sequences for therapeutic editing







ADVANCED EDITING

Improve efficiency of gene correction and multiplexing

STEM CELL ENGINEERING

Expand applications of gene-edited stem cells to treat disease

Fifty-Percent Ownership of Casebia Therapeutics

Committed IP
for select indications

Committed $370M
$265M to Casebia and $105M to CRISPR

THERAPEUTIC FOCUS AREAS

Hematology

Cardiology

Ophthalmology

Joint research on platform technology – protein engineering, delivery, etc.

CRISPR has full access at no cost to *all new* IP for use within the field of human therapeutics

Foundational Intellectual Property Landscape

	Foundational IP estate		Broad IP estate
Patent Filings	**EMMANUELLE CHARPENTIER**	**UC BERKELEY / U. VIENNA**	**BROAD INSTITUTE**
Human Therapeutics Licensees	CRISPR THERAPEUTICS	Intellia THERAPEUTICS via CARIBOU BIOSCIENCES	editas MEDICINE
Strategic Investors	Celgene, gsk		
Partners & Total Deal Size	BAYER, VERTEX, >$3B	NOVARTIS, REGENERON, >$3B	JUNO THERAPEUTICS, Allergan, <$2B

- Direct license to foundational IP covering all human therapeutic fields; term through 2033
- Four large pharma partnerships indicate strength of the Charpentier / Berkeley foundational IP estate
- Access to Vilnius IP estate through invention management agreement

Strong U.S. and Global Foundational IP Position

UNITED STATES

Charpentier / UCB / U. Vienna granted wide-ranging patent; multiple applications progressing

- Wide-ranging patent granted in U.S.
- Multiple patent applications moving forward in parallel with both broad and narrow claims
- Appeal ongoing in Federal Appeals Court to overturn Feb 2017 PTAB decision to end the first interference on technical grounds – decision expected in 2018

EUROPE AND GLOBAL

Charpentier / UCB / U. Vienna granted foundational patents, including use in eukaryotes

- 3 patents granted between EU and U.K. include single-guide RNA and uses in all settings
- Patents of broad scope granted in Japan, China, Singapore, Australia, New Zealand, Mexico, and elsewhere
- Advancing applications globally in ~80 jurisdictions worldwide with both broad and narrow claims

Experienced Management Team

SAM KULKARNI, PHD
Chief Executive Officer
Partner, McKinsey & Company

RODGER NOVAK, MD
President & Chairman
Head of Anti-Infectives R&D, Sanofi

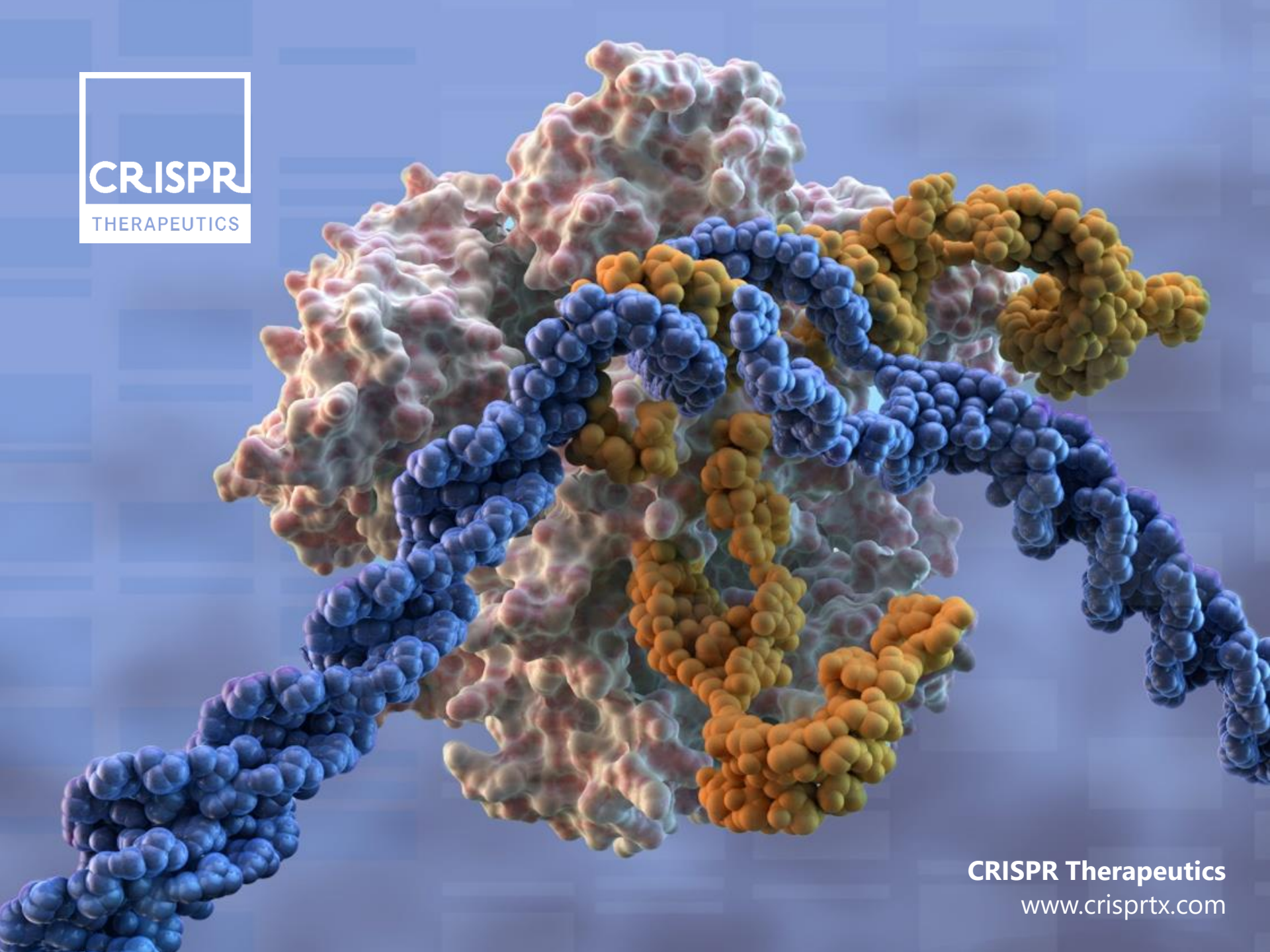
TONY HO, MD
Head of Research & Development
Head of Oncology Innovation, AstraZeneca

JIM KASINGER, JD
General Counsel & Corporate Secretary
General Counsel, Moderna

LAWRENCE KLEIN, PHD
Head of Business Development & Strategy
Associate Partner, McKinsey & Company

MIKE TOMSICEK, MBA
Chief Financial Officer
Chief Financial Officer, Abiomed

SHELBY WALKER, JD
Head of Intellectual Property
Chief IP Counsel, Dyax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