HELIX biopharma

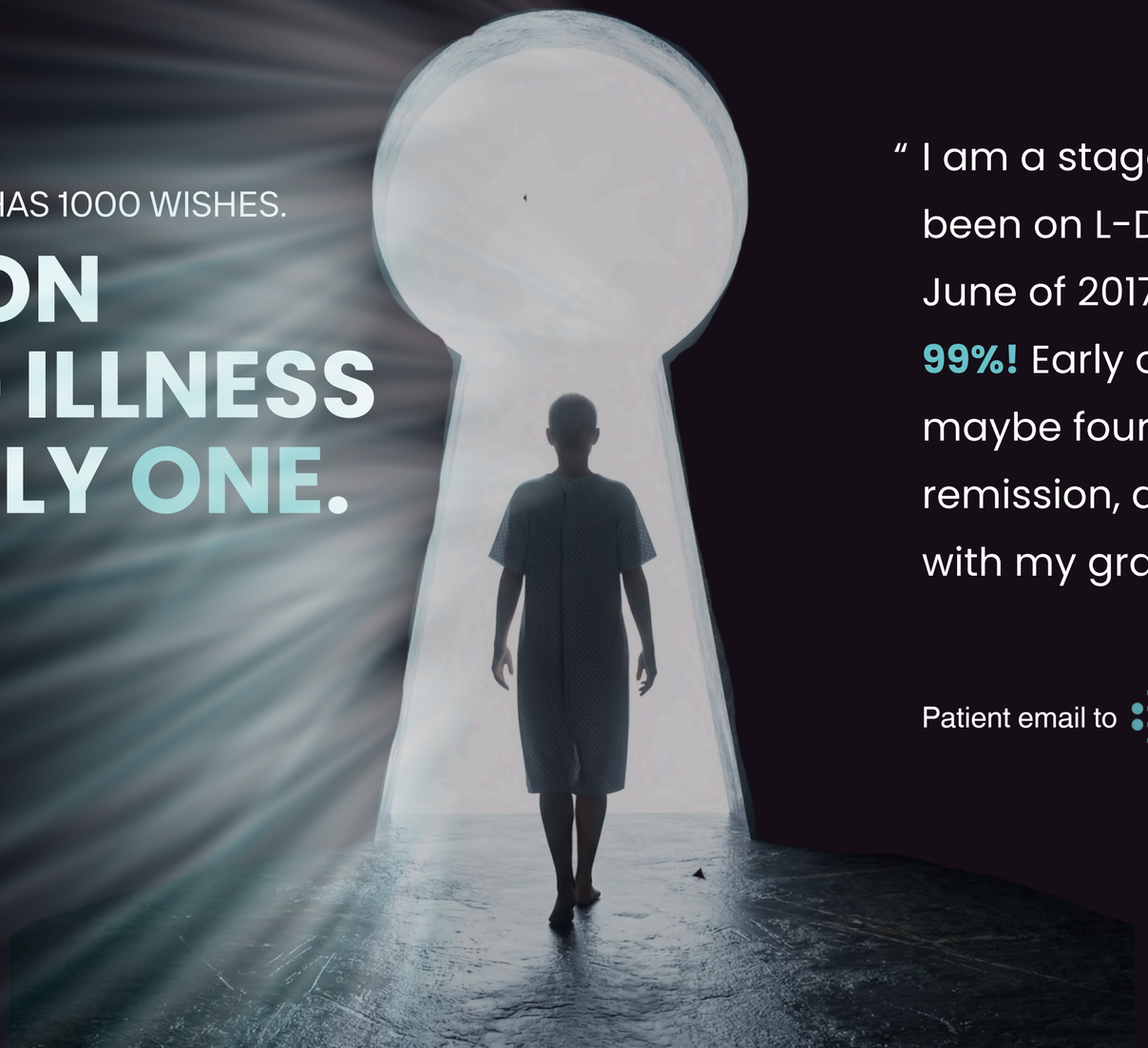
Shaping a near future where today's hard-to-treat cancers are *vincible*.

As featured in: International Business Times. USA TODAY (US Audiences Only)

PUBLIC Company Presentation, Q4 2026

A HEALTHY PERSON HAS 1000 WISHES.

A PERSON FACING ILLNESS HAS ONLY ONE.



" I am a stage 4 lung cancer patient and have been on L-DOS47 [with chemotherapy] since June of 2017. **To date my tumor has shrunk by 99%!** Early on in my diagnosis I was told I had maybe four months to live. I am now in remission, and looking forward to many years with my grandchildren. "

Patient email to HELIX biopharma, January 2018

INVESTMENT HIGHLIGHTS

Helix BioPharma is on a mission to level the playing field against cancer's biggest, most urgent challenges.

INNOVATING FROM STRENGTH

1. Assets with high potential and a head start
2. Management team with a track record of success
3. USD 140M raised to date

FOCUSED, AMBITIOUS PLAN AHEAD

1. Nasdaq uplisting and public offering (USD25M)
2. Initiate two clinical studies within next 24 months
3. Near-term partnering/exits

PIPELINE	LEAD INDICATION	NEXT MILESTONE	POTENTIAL
* **L-DOS47** Antibody-Enzyme Conjugate (AEC)	Non-small cell lung cancer	**Phase Ib/II**	≥30% efficacy added to checkpoint inhibitors
C6 Antibody-Drug Conjugates (ADCs)	Solid tumors	**Patent filings**	Overcome resistance, maximize efficacy
* **LEUMUNA** Small molecule, FDA Orphan status	Leukemia relapse	**Phase I/II IND**	Long-term remission (2+ years) or cure
GEMCEDA First-in-class oral chemotherapy	Advanced solid tumors	**Phase I/II IND**	Significant increase in progression-free survival

RAISING

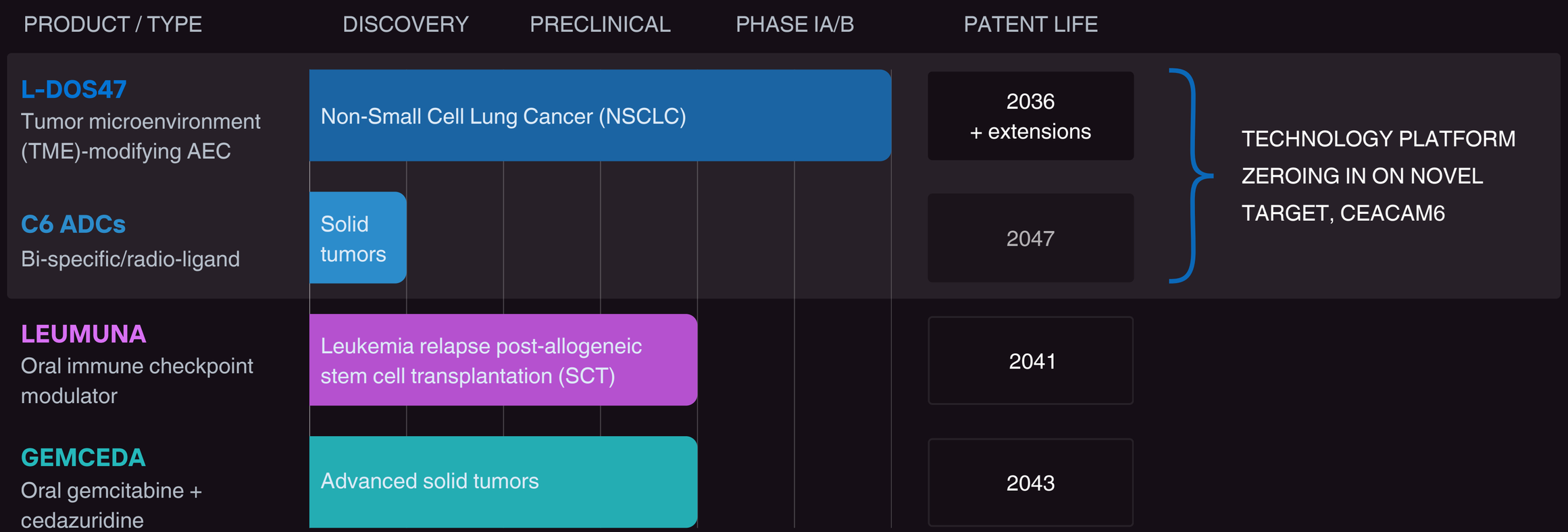
USD 80 million

to reach major value inflection points and bring much-needed therapies to patients with hard-to-treat cancers.

*Priority projects nearest to major value inflection points.

OUR PIPELINE

Diverse, clinical-stage pipeline of candidates with great potential and a head start, honed into first- and best-in-class oncology medicines.



LEAD INDICATIONS

Prevalent and hard-to-treat cancers made vincible by novel therapies that rise to the challenge.

HOW WE WANT TO MOVE THE NEEDLE

ADD ≥30% EFFICACY

to immune checkpoint inhibitors (ICIs) standard of care

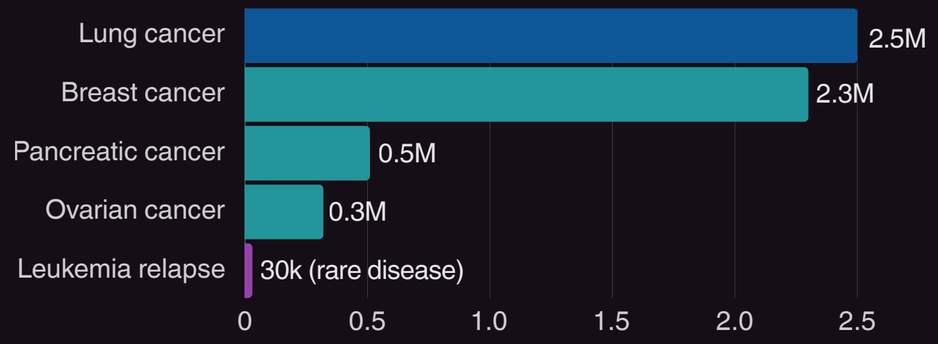
CURE OR LONG-TERM SURVIVAL

of 2+ years for patients relapsing with leukemia

REDEFINE MAINENTANCE THERAPY OUTCOMES

and significantly increase progression-free survival

LEAD INDICATIONS, GLOBAL INCIDENCE (MILLIONS)



HIGH MORTALITY (5 YEARS FROM DIAGNOSIS):

WHO GLOBOCAN, 2022. American Cancer Society (2024). Brandwein et al, 2020. Pancreatic Cancer Action Network (2024).

INVESTMENT & RETURN

USD 80M to achieve major project milestones and value inflection points for L-DOS47 and LEUMUNA as priority projects.

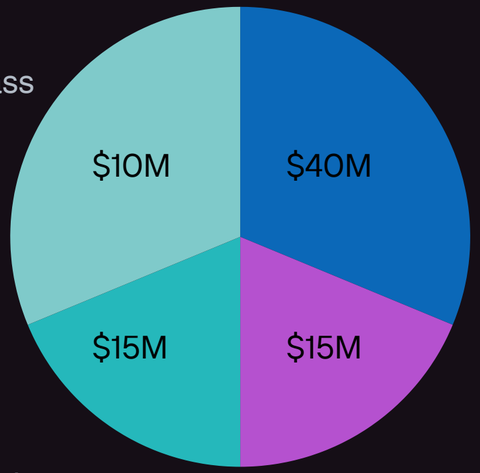
USE OF PROCEEDS OVER THE NEXT 36 MONTHS

CORPORATE

- Grow world-class team
- Business development

CEACAM6 PLATFORM

- Phase IB + Phase II randomized study in NSCLC
- C6 ADCs preclinical and IND



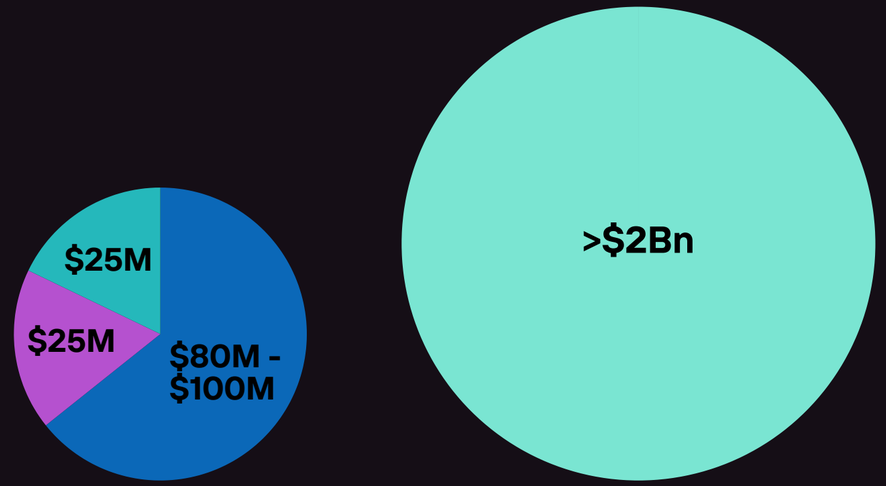
GEMCEDA

- Phase I\II study in advanced solid tumour

LR 09

- Phase I\II study in leukemia relapse

THE WHOLE IS GREATER THAN THE SUM OF ITS PARTS



PRESENT VALUE
(market cap & private valuations)

FUTURE VALUE
HELIX 2.0

WHO WE ARE

A team built to translate science into value in oncology.

LEADERSHIP & CORPORATE AFFAIRS

Thomas Mehrling, MD, PhD
Chief Executive Officer

Veronika Kandziora
Chief Operating Officer

Rohit Babbar, CPA, CA
Chief Financial Officer

Jessica Kourniaktis, DPhil
Director of Communications

Helen Middleton, LPC
General Counsel

SCIENTIFIC TEAM

Markus Loeffler, MD, MBA
Chief Medical Officer

Davide Guggi, PhD
Chief Technology Officer

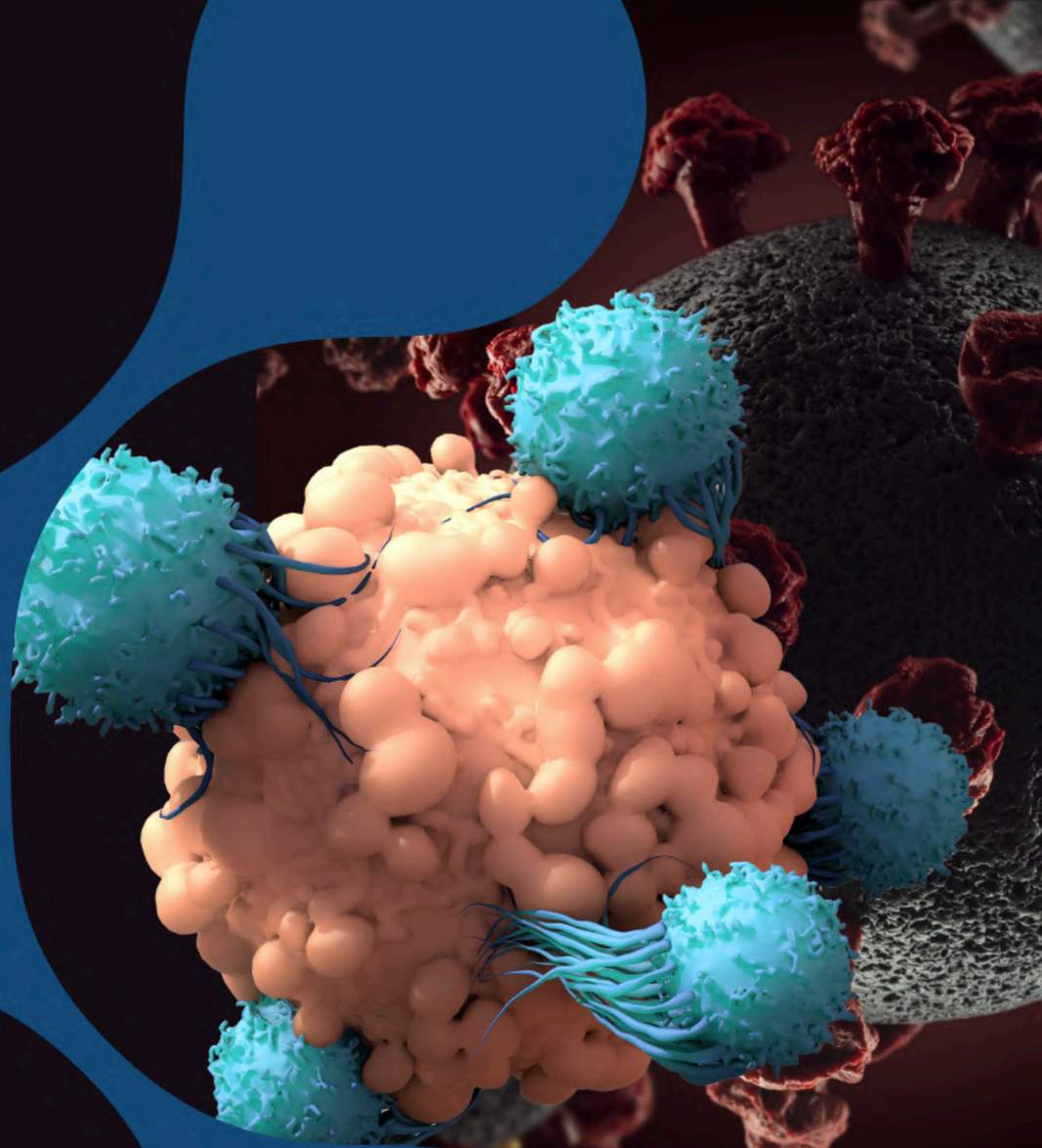
David Browning, MBA
VP of Clinical Operations

Brenda Lee, PhD
Director of Clinical Operations

Jonathan Davis, PhD
Director of ADC Discovery

L-DOS47

A first-in-class, clinical-stage antibody-enzyme conjugate (AEC) delivering **a game-changing assist to anti-tumor immunity and blockbuster cancer immunotherapies**.

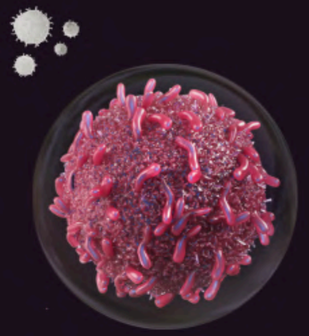


THE PROBLEM

TUMOR ACIDOSIS

The success of immune checkpoint inhibitors (ICIs) **depends on the availability of functioning immune cells** to mobilize against the tumor.

But in the **acidic microenvironment** of solid tumors, immune cells are blocked, suppressed and starved of energy, leaving ICIs with no functional immune population to mobilize.



70% of cancer patients

don't respond to immunotherapy.[1]

Immunologically "cold" (immune-excluded) tumors

exhibit poorest responses to immune checkpoint inhibitors.[2]

The acidic tumor microenvironment (TME)

is a major driver of immune-exclusion in solid tumors.[3]

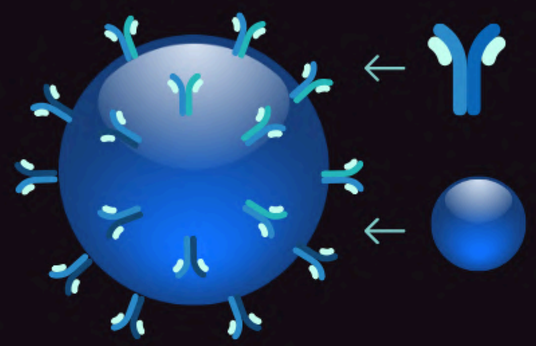
1) Ramos et al, 2022. 2) Zheng et al, 2023. 3) Ngwa et al, 2019.

THE SOLUTION

TUMOR DEFENCE BREAKER™

L-DOS47

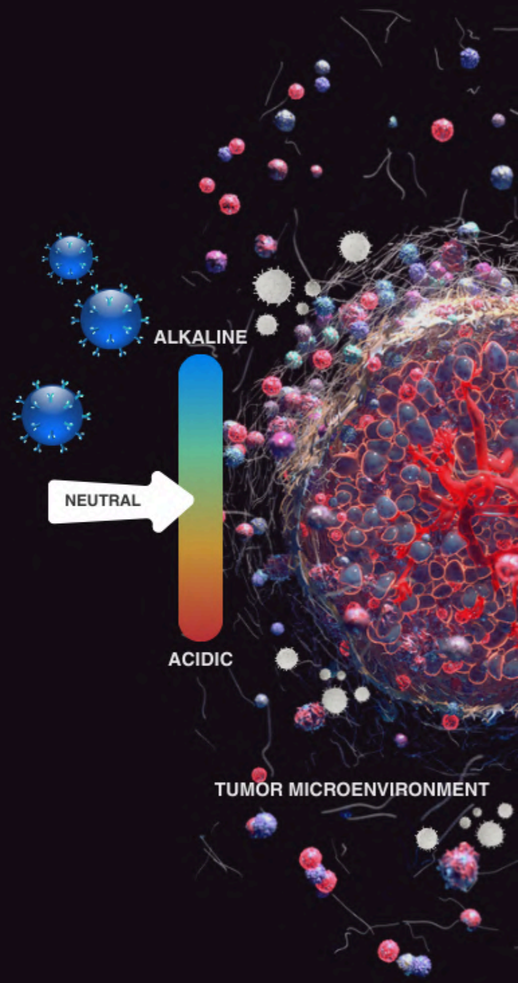
A first-in-class AEC that **neutralizes the acidic pH of the TME, helping turn immunologically cold tumors "hot",** and priming them for increased sensitivity to cancer immunotherapy.



L-DOS47

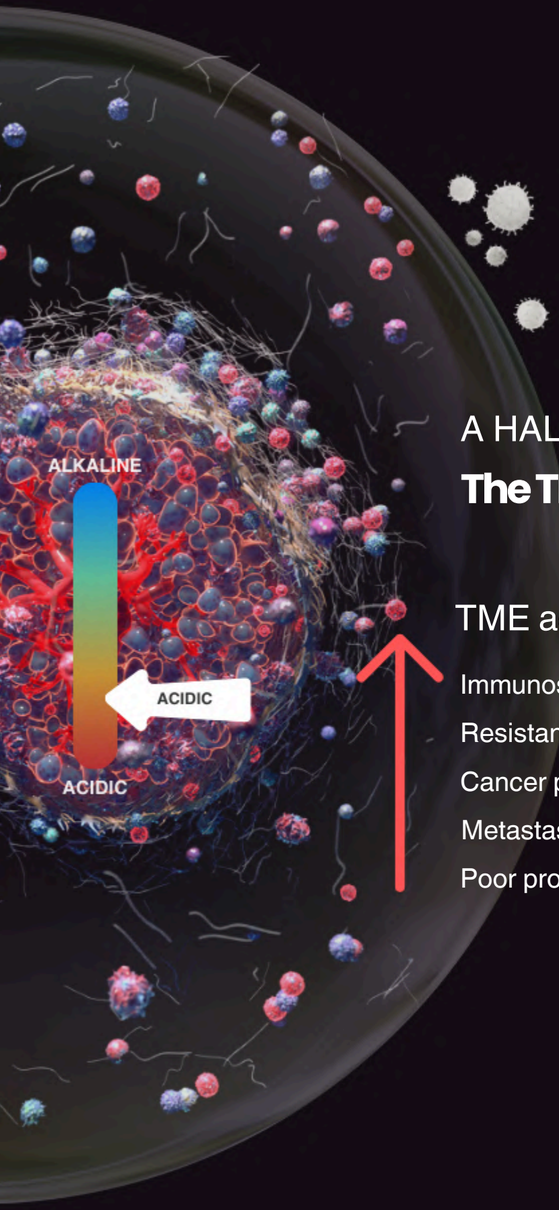
Camelid nanobodies
High binding affinity to CEACAM6.

Urease enzyme
Catalyzes urea breakdown into ammonia and CO_2, neutralizing the pH of the TME.



CEACAM6: Carcinoembryonic antigen-related cell adhesion molecule 6.

MECHANISM OF ACTION

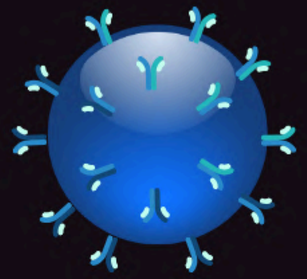


A HALLMARK OF CANCER

The TME is acidic.

TME acidosis leads to:

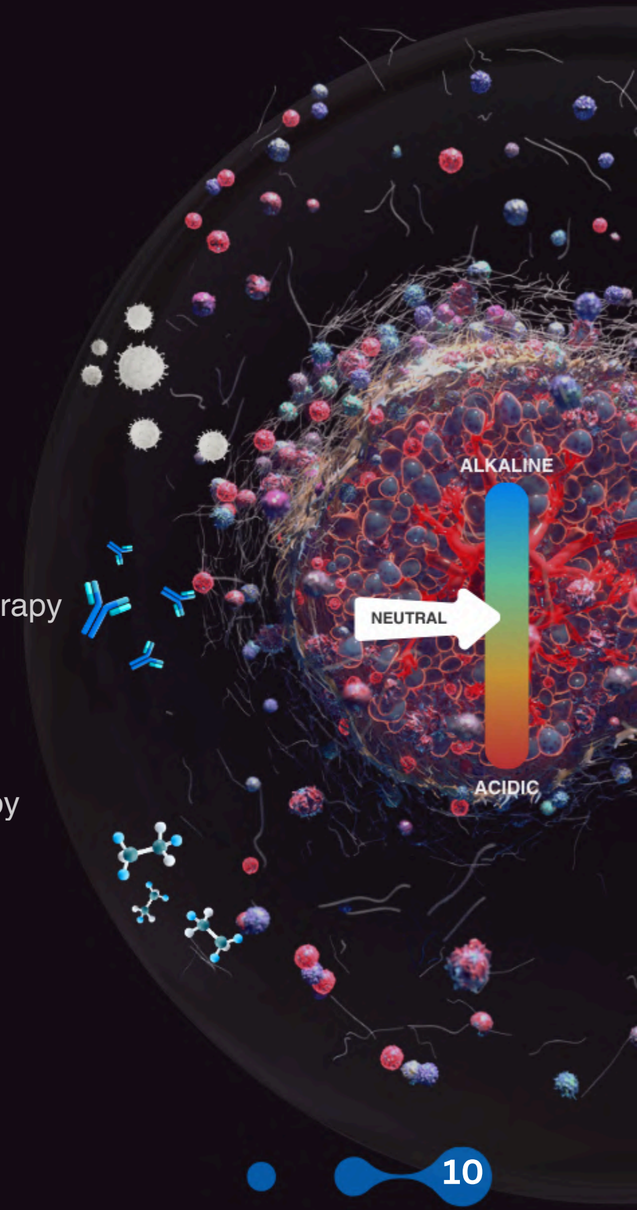
- Immunosuppression (“cold” tumors)
- Resistance to treatment
- Cancer proliferation
- Metastasis
- Poor prognosis



L-DOS47

neutralizes tumor acidity, taking the brakes off anti-tumor immunity and delivering a game-changing assist to ICIs.

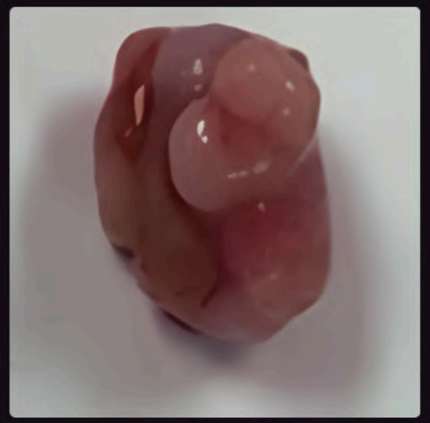
- T Cells
- Immunotherapy
- Chemotherapy



See MoA video.

A FORCE MULTIPLIER FOR ANTI-PD-1 ANTIBODIES

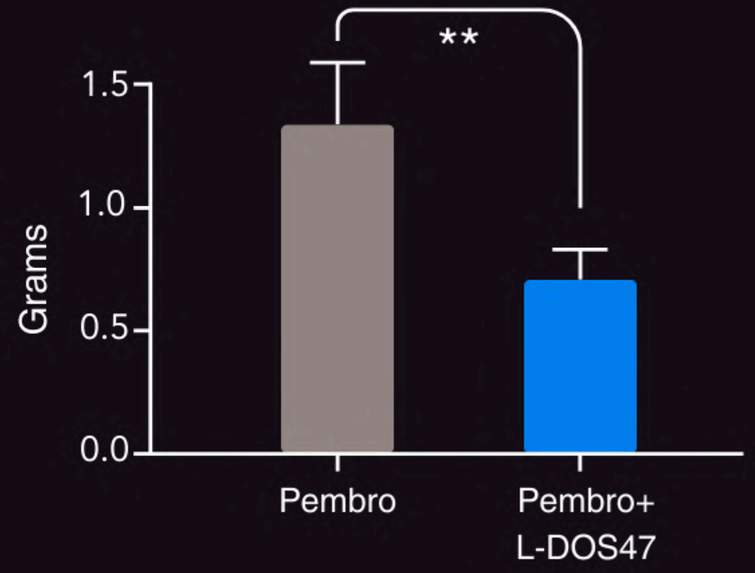
Anti-PD-1 + L-DOS47 synergistically and significantly reduces tumor growth, volume and weight compared to anti-PD-1 alone in 4 weeks in pancreatic cancer mouse models.



424 mm^3
Pembro monotherapy

129 mm^3
Pembro + L-DOS47

-70% greater tumor volume reduction
with L-DOS47 + Anti-PD-1 vs. Anti-PD-1 alone.



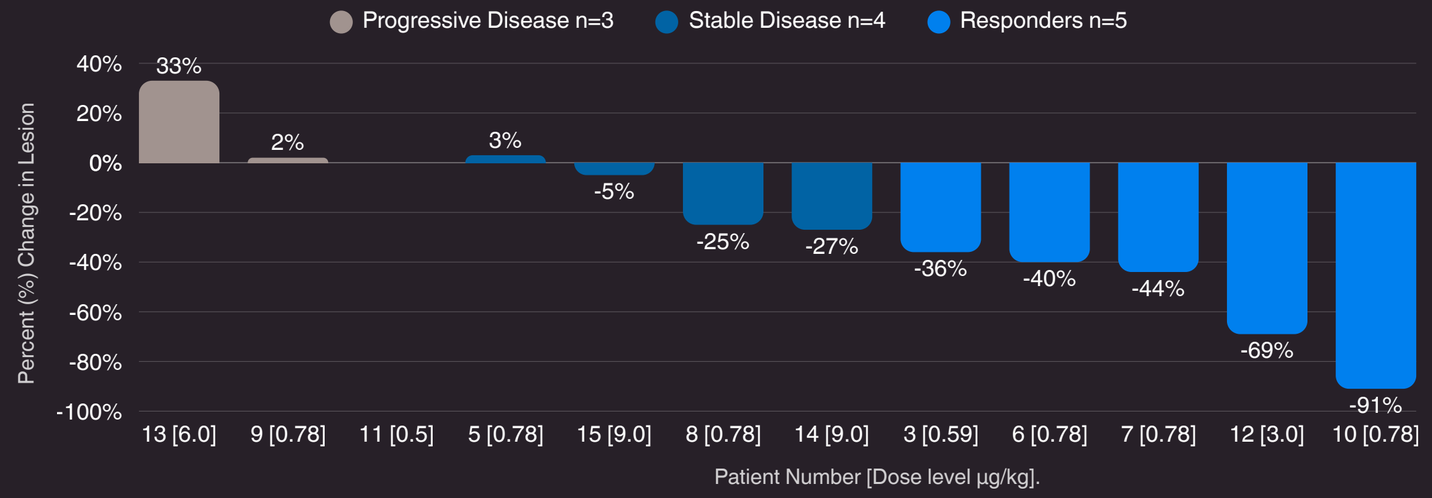
-50% greater tumor weight reduction
with L-DOS47 + Anti-PD-1 vs. Anti-PD-1 alone.

Jardim-Perassi, BV et al, Biomedicines 2024.

CLINICALLY SAFE AND EFFECTIVE WITH CHEMO

L-DOS47 in combination with Pemetrexed/Carboplatin delivers 75% overall clinical benefit in a Phase IB, open-label dose-escalation study in heavily pre-treated patients with Stage IV NSCLC.

EFFICACY & SAFETY — **Best % Change in Lesion Size from Baseline** (patients n=12)



→ No dose-limiting toxicities at doses ≤9.0 µg/kg (patients n=14).

4 cycles of L-DOS47 (Days 1, 8 & 15 of each cycle) in combination with pemetrexed (500 mg/m2) + carboplatin (on Day 1 of each cycle). Patients who did not experience unacceptable toxicities continued to receive L-DOS47 on the same schedule until there was no longer a clinical benefit.

Study population: **Patients:** n=14 **Mean age:** 63.5 **Sex:** 50% female **NSC carcinoma:** n=5 **Adenocarcinoma, NOS:** n=9

STUDY HIGHLIGHTS

75% overall clinical benefit

141 days median duration of clinical benefit

42% overall response

187 days median duration of response

1 near complete remission

337 days maximum duration of response

Piha-Paul, S et al, JTO Clin Res Rep. 2022

TIMELY & CLOSE TO THE FINISH LINE

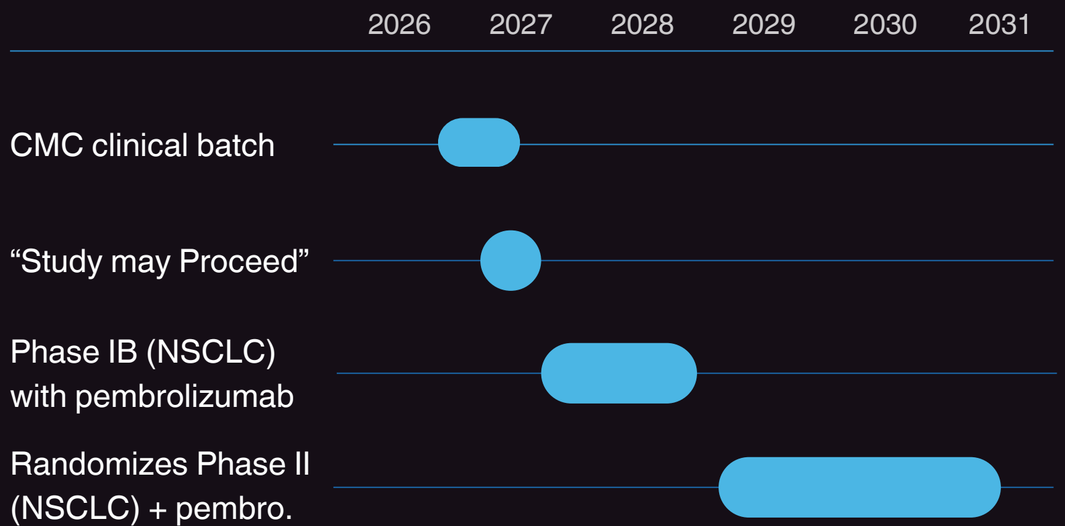
L-DOS47 STRENGTHS

- First-in-class TME AEC
- Phase Ib completed
- Results highly encouraging
- Combination therapy with ICIs
- Patents to 2036 + extensions
- FDA supports ICI combo
- NSCLC = High unmet need

L-DOS47 OPPORTUNITIES

- Significant improvement in PFS
- Significant improvement in OS
- ICI market share expansion
- Other solid tumors

L-DOS47 NEXT STEPS



CAPITAL REQUIREMENT

USD 40M

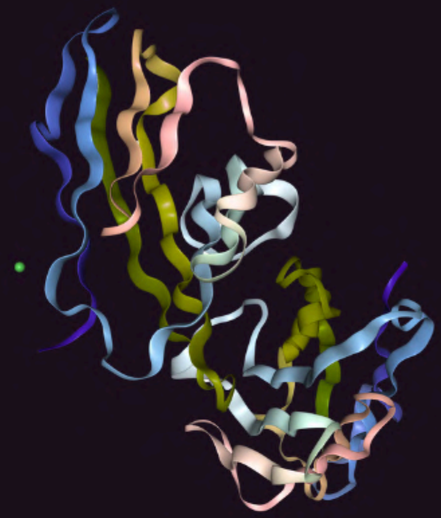
(2027–31)

THE BIGGER PICTURE

CEACAM6

CEACAM6 (carcinoembryonic antigen-related cell adhesion 6) is a cell-surface protein overexpressed on hard-to-treat solid tumors and **a highly promising target** for antibody-based therapies.[1]

Helix brings a **first-mover advantage in CEACAM6**, with L-DOS47 engineered to bind this antigen, and is expanding its **technology platform around this target** as part of its long-range plan.



Overexpressed in major cancers

CEACAM6 is significantly low in healthy tissue.

Associated with poorer patient survival

including disease-free survival (DFS) and overall survival (OS).

Linked to malignancy progression

including cancer proliferation and metastasis.

1) Zhao et al, 2024; Wu et al, 2024.

PRODUCT 2, CEACAM6 PLATFORM

LEVERAGING RADIO-LIGAND TECHNOLOGY IN DISCOVERY

CEACAM6 Product 2

CEACAM6-RL-PDAC (radio-ligand targeting CEACAM6-expressing pancreatic adenocarcinoma).

Design

Single chain camelid nanobody with CEACAM6 high binding affinity.

Radio-Isotope

Alpha emitter, carefully selected to maximize tumor penetration and efficacy.

PRODUCTS 3 & 4, CEACAM6 PLATFORM

THE PROMISE OF OUR DISCOVERY ADCs

Carefully-designed ADCs capitalising on latest, state-of-the-art technology.

CEACAM6 Products 3 & 4

CEACAM6-GIT (Gastrointestinal)
CEACAM6-GYN (Gynecological)

Conjugation

Newest linker system, ensuring systemic stability.

Design

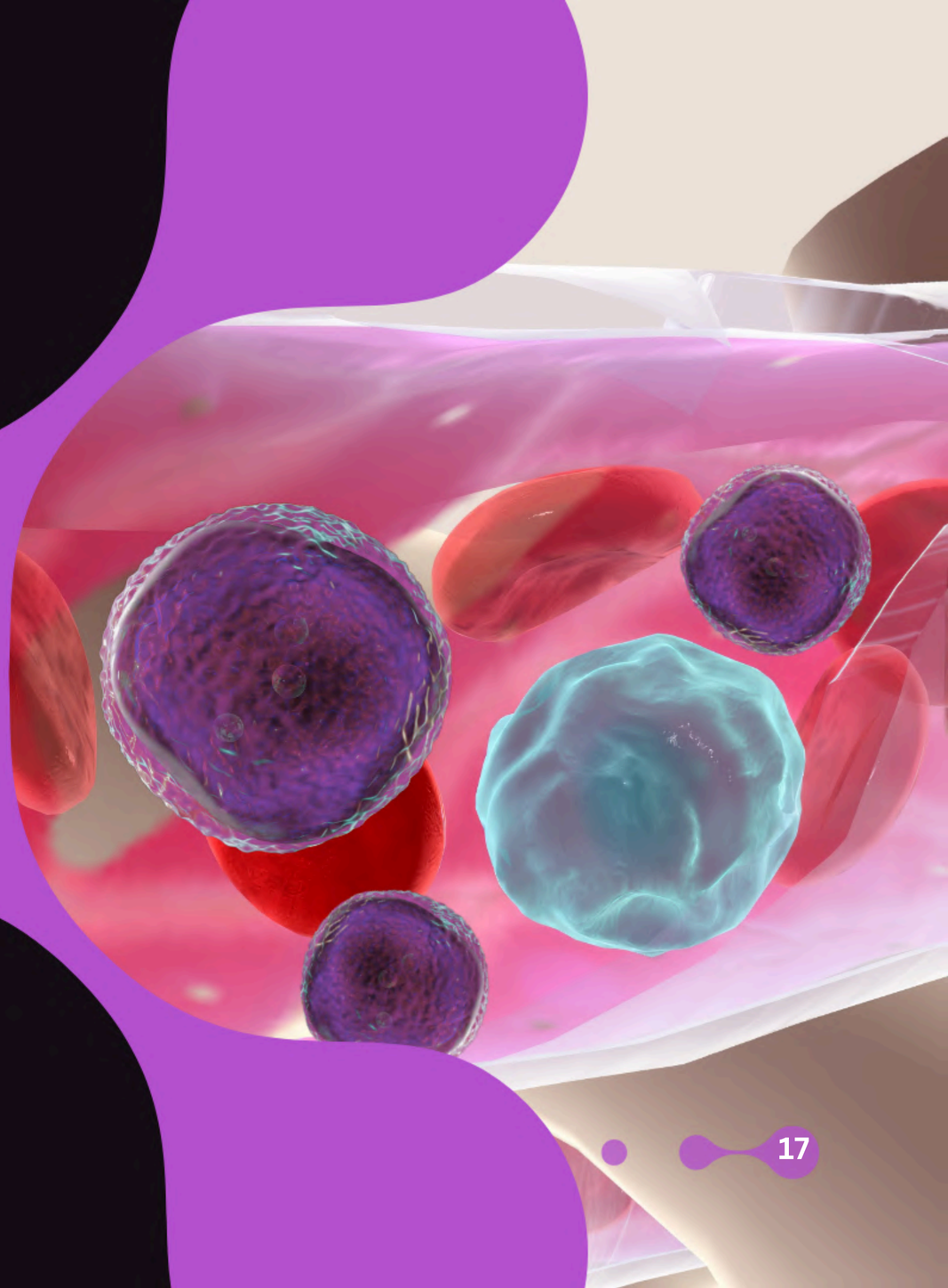
Bi-specific, maximising target engagement.

Payloads

Multi-payload - High DAR, maximising efficacy, avoiding resistance.

LEUMUNA™

An oral immune checkpoint modulator to **bring long-term remission within reach** for patients relapsing with leukemia.

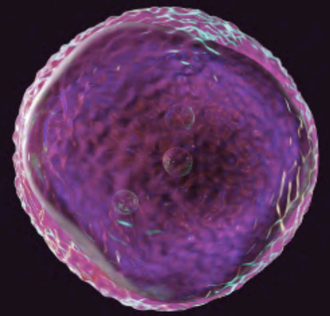


THE PROBLEM

LEUKEMIA RELAPSE

Allogeneic stem cell transplantation (allo-SCT) offers a potentially life-saving treatment for patients with hematological malignancies.

But nothing is more devastating than seeing the malignancy return, **stealing away the hope of remission** just when it seemed within reach.



More than 60,000

patients undergo allo-SCT each year.[1]

Up to 30% or 18,000

of patients relapse after allo-SCT.[2]

Survival: ~4 months

with only 21% of patients alive after 1 year.[3]

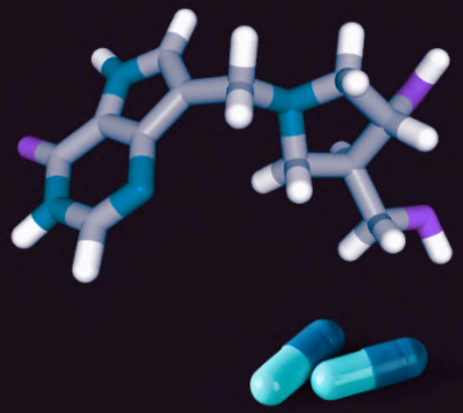
1) Gyurkocza, Rezvani & Storb, 2014. 2) Chen et al, 2023. 3) Michallet et al, 2011.

THE SOLUTION

LEUMUNA™

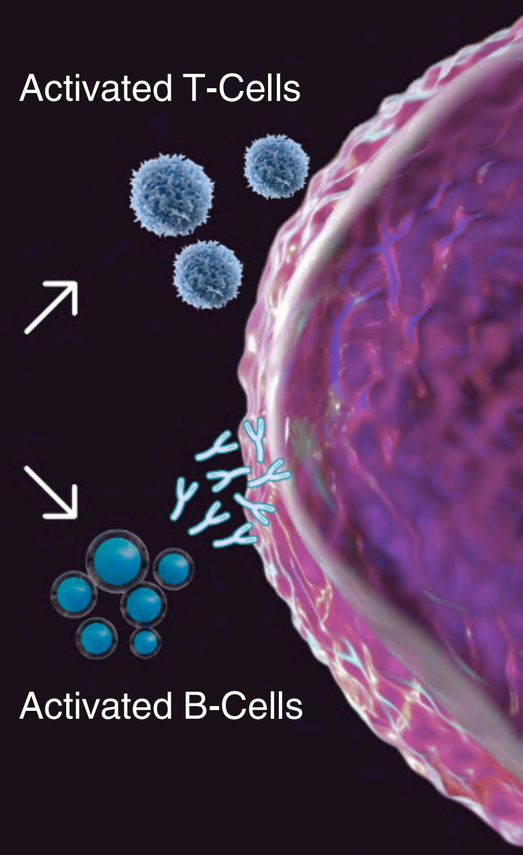
A pre-IND, first-in-class oral immune checkpoint modulator and inhibitor of PNP to initiate **graft-versus-leukemia (GvL) effect** in patients relapsing with leukemia after allogeneic SCT.

GvL is the most effective path to long-term remission,[1] making LEUMUNA potentially curative in a rare disease with **no standard of care (SoC)**.



LEUMUNA

Activates transplanted immune system to fight resurging leukemia



PNP: Purine Nucleoside Phosphorylase.

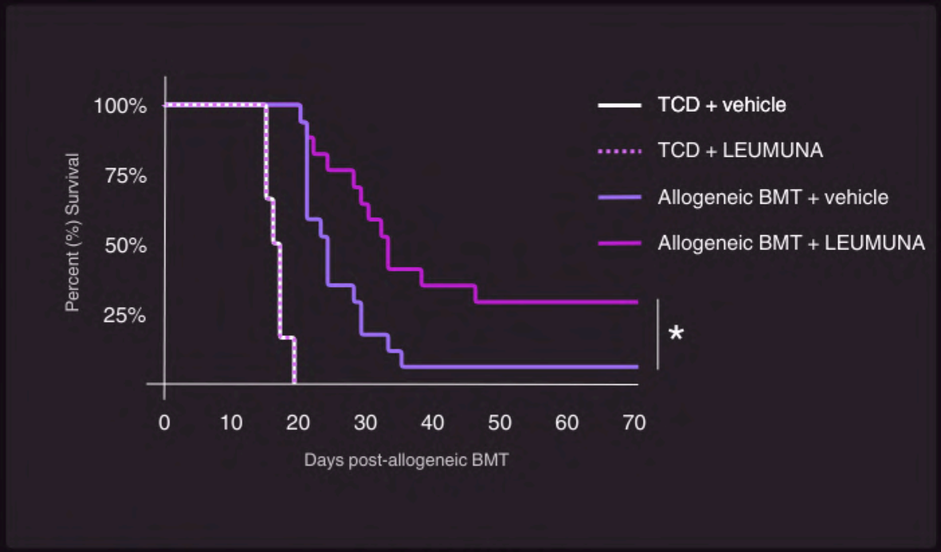
1) Mauer & Antin, 2024.

EVIDENCE WITH LEUMUNA

LEUMUNA significantly reduces risk of relapse mortality in preclinical minor-MHC mismatch B Cell Acute leukemia model.

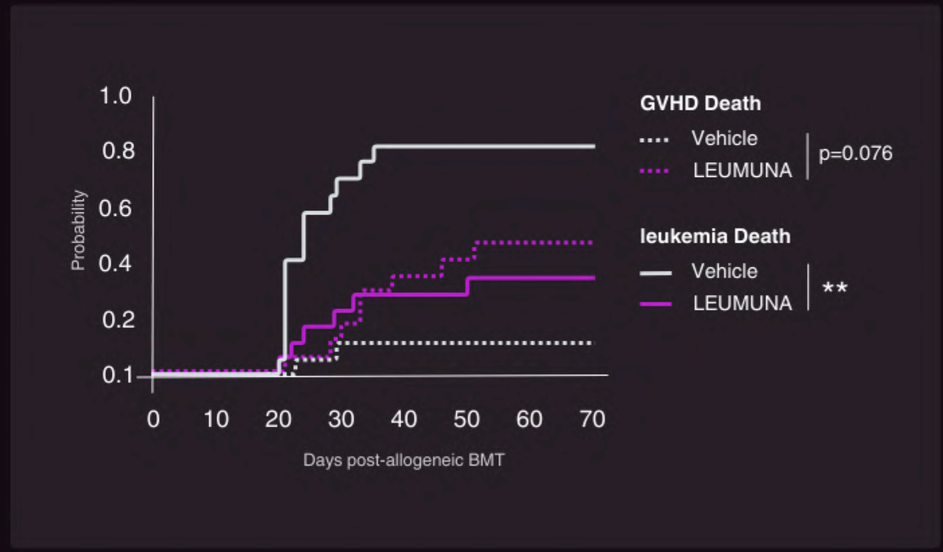
1) OVERALL SURVIVAL

Improvement in survival with LEUMUNA **is due to T-cell activation and initiation of graft-versus-leukemia (GvL) effect**.



2) COMPETING RISK ANALYSIS

Risk of graft-versus-host disease (GVHD) mortality outweighed by **statistically-significant reduction leukemic death risk with LEUMUNA.**



Unpublished data; study carried out at the Fred Hutchinson Cancer Center.

TCD: T-Cell Depleted bone marrow.

BMT: Bone Marrow Transplantation.

HISTORICAL CLINICAL DATA

Predecessor compound, Ulodesine (BCX4208), developed in gout and psoriasis, and analog, forodesine hydrochloride.

BCX4208: OUTSTANDING SAFETY AND TOLERABILITY

Demonstrated in Phase I & II studies in 500+ volunteers.

Infectious Adverse Events (AEs)	**Placebo (n=56)**	5mg (n=56)	10mg (n=56)	20mg (n=56)	**40mg (n=54)**
Any infections AEs N(%)	**11 (20%)**	10 (18%)	10 (18%)	9 (16%)	**11 (20%)**
Typical cold symptoms	6 (11%)	7 (13%)	2 (4%)	4 (8%)	4 (7%)
Lower respiratory tract	2 (4%)	0	1 (2%)	0	1 (2%)
Bacterial/Potentially bacterial	5 (9%)	2 (14%)	9 (16%)	5 (9%)	7 (13%)
Viral/Potentially viral	10 (18%)	9 (16%)	3 (5%)	4 (8%)	6 (11%)
Fungal/Potentially fungal	1 (2%)	1 (2%)	1 (2%)	1 (2%)	1 (2%)

Long-Term Safety: A Phase 2 BCX4208 24-Week Blinded Safety Extension and Vaccine Challenge Study. Presented at EULAR, Berlin, June 6 – 9 2012.

COMPLETE REMISSION ACHIEVED

A 3-year old pediatric patient was cured of relapsed T-Cell Acute Lymphoblastic Leukemia (T-ALL) with PNP inhibitor, Forodesine.

You can view Katie Lambertson's patient case, titled *When a Drug Becomes a Child's Last Hope for T-Cell Leukaemia* (Albert Einstein College of Medicine) here.

Forodesine, which is scientifically and pharmacologically interchangeable with LEUMUNA, was later discontinued for commercial reasons.

Gore L, et al.. Semin Oncol. 2007;34(6 Suppl 5):S35-39. doi:10.1053/j.seminoncol.2007.11.005.

LEUMUNA FACTS & PROSPECTS

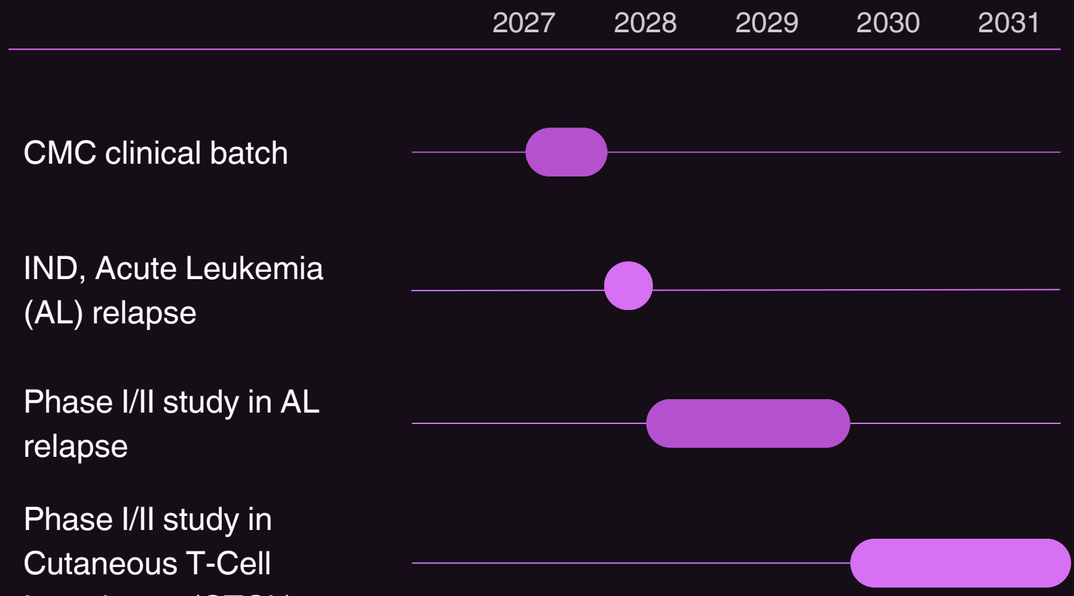
LEUMUNA STRENGTHS

- FDA Orphan status
- CoM Patent (exp. 2041)
- Supporting clinical evidence
- Established safety (n=500)
- First-in-class CP modulator
- Easy, oral administration

LEUMUNA OPPORTUNITIES

- Potential 2+ yrs. OS or cure
- Poised to become SoC
- Breakthrough potential and accelerated approval
- Orphan pricing of USD 180k/patient/year.
- Upsides (other liquid tumors; licensing agreement in place)

LEUMUNA NEXT STEPS



CAPITAL REQUIREMENT

USD 28M

(2027–31)

OS: Overall Survival.

GEMCEDA™

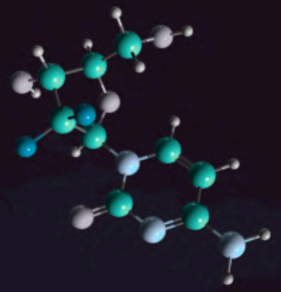
A first-in-class oral gemcitabine to enrich the spectrum of **disease-limiting and life-enhancing outcomes** for patients whose cancer has progressed.

THE PROBLEM

ORAL GEMCITABINE

Gemcitabine is a WHO-designated Essential Medicine used to treat one-third of all cancers and is among the most widely prescribed therapies worldwide.[1]

But with intravenous (IV) delivery as the only available option, its use in maintenance, metronomic schedules, and combinations is severely limited.



More than 30%

of the 900 chemotherapy agents in development are oral agents, to improve access to care.[2]

Oral chemotherapy

opens the door to maintenance therapy, metronomic dosing, and stronger combination outcomes.[3]

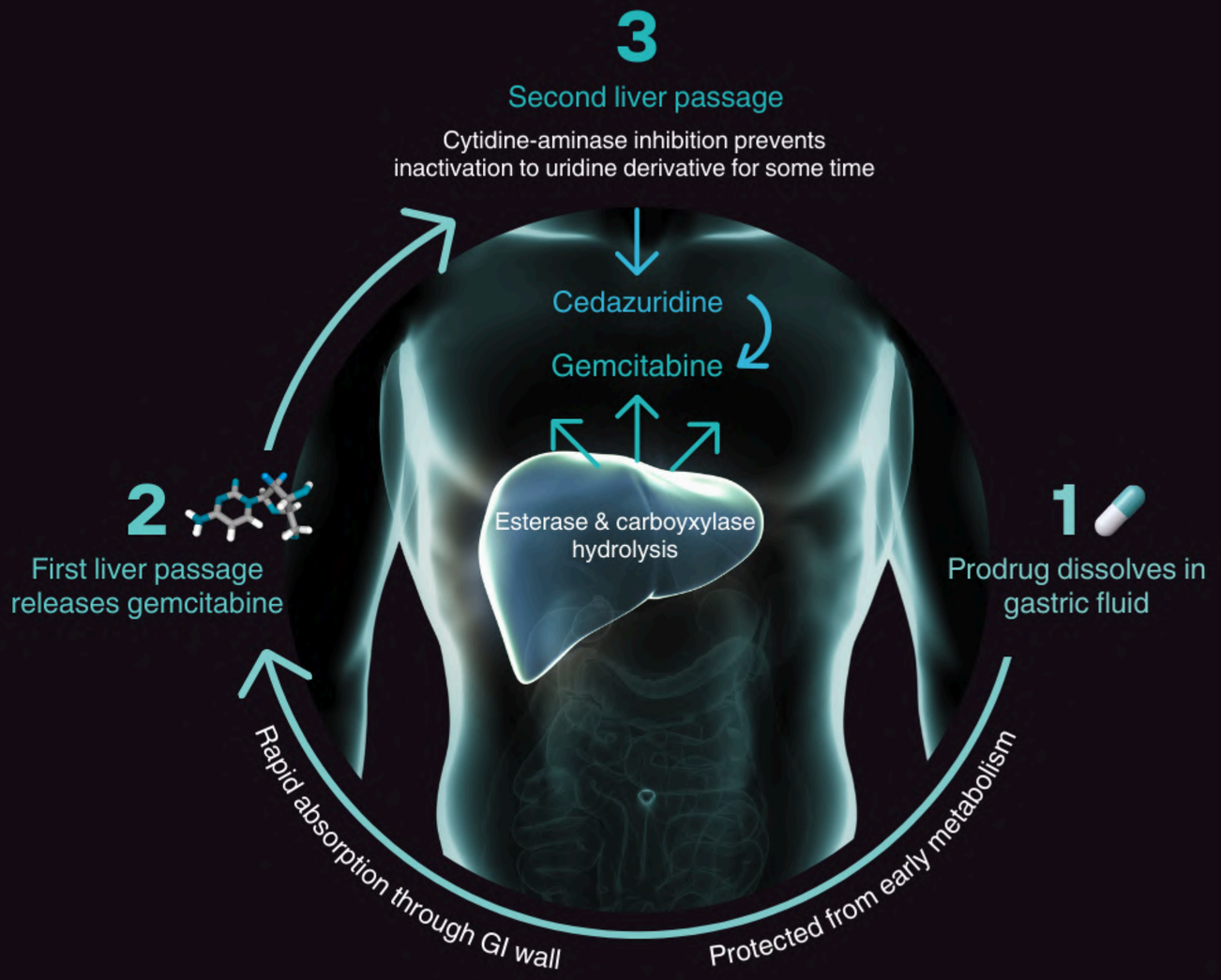
10% oral bioavailability

of gemcitabine has made it nearly impossible to create an oral form of this essential drug.[4]

1) Ciccolini et al, 2016; Paroha et al, 2021. 2) HOPA, 2024. 3) Muraro et al, 2023. 4) Thompson et al, 2020.

GEMCEDA

A pre-IND, first-in-class oral gemcitabine prodrug combined with cedazuridine, **with bioavailability on par with IV (90%)**, for metronomic therapy to control tumor growth and preserve quality of life.



GEMCITABINE ORAL CHEMOTHERAPY

Target indications with biomarkers predictive of gemcitabine efficacy.

High-grade Serous Ovarian Cancer*

High vs low replication stress (RB1, CDKN2A loss, or surplus of CCNE1, KRAS, MYC).

Combination with PARP or ATR inhibitor.

Pancreatic Ductal Adenocarcinoma

Use GemciTest® to predict gemcitabine response.

Non-Small Cell Lung Cancer (NSCLC)

Determine serum CDA levels for oral gemcitabine maintenance after Pt/gem induction.**

Combination with PD-1/PD-L1 inhibitor sintilimab.***

Injury signals from tumor cells more immunogenic than killing tumor cells.****

* Konstantinopoulos et al, 2021.
** Tibaldi et al, 2018.
*** ASCO Post, 2021.
**** Sriram et al, 2021.

GEMCEDA FACTS & PROSPECTS

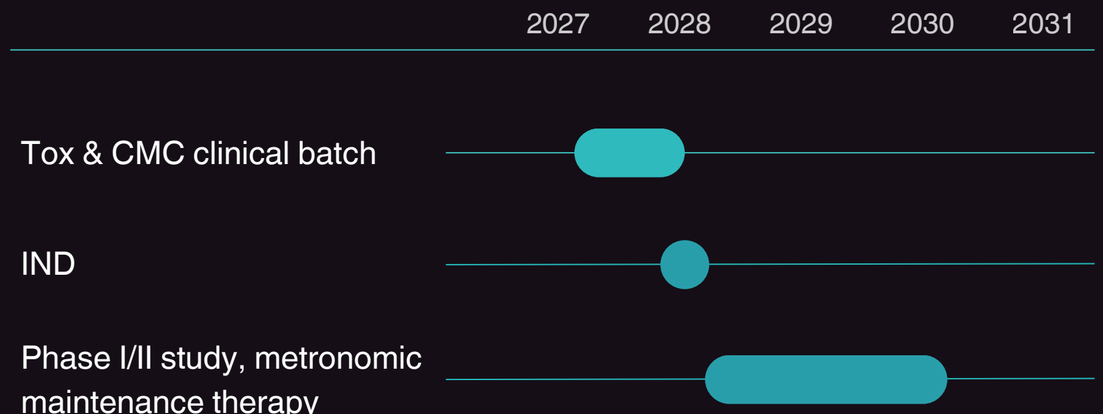
GEMCEDA STRENGTHS

- First-in-class oral gemcitabine
- Oral bioavailability ≈ IV
- CoM Patent (exp. 2043)
- Established manufacturing
- Low COGs
- Easy, oral administration

GEMCEDA OPPORTUNITIES

- IV gem. treats 1/3 of cancers
- Regulatory 505(b)2 pathway
- Maintenance therapy
- Combination therapy
- Partnering & non-dilutive financing opportunities
- Gemcitabine market size: $789M (2024) → $1.5Bn (2034)[1]

GEMCEDA NEXT STEPS



CAPITAL REQUIREMENT

USD 19M

(2027–30)

1) Global Market Insights, Mar. 2025.

THE BOTTOM LINE

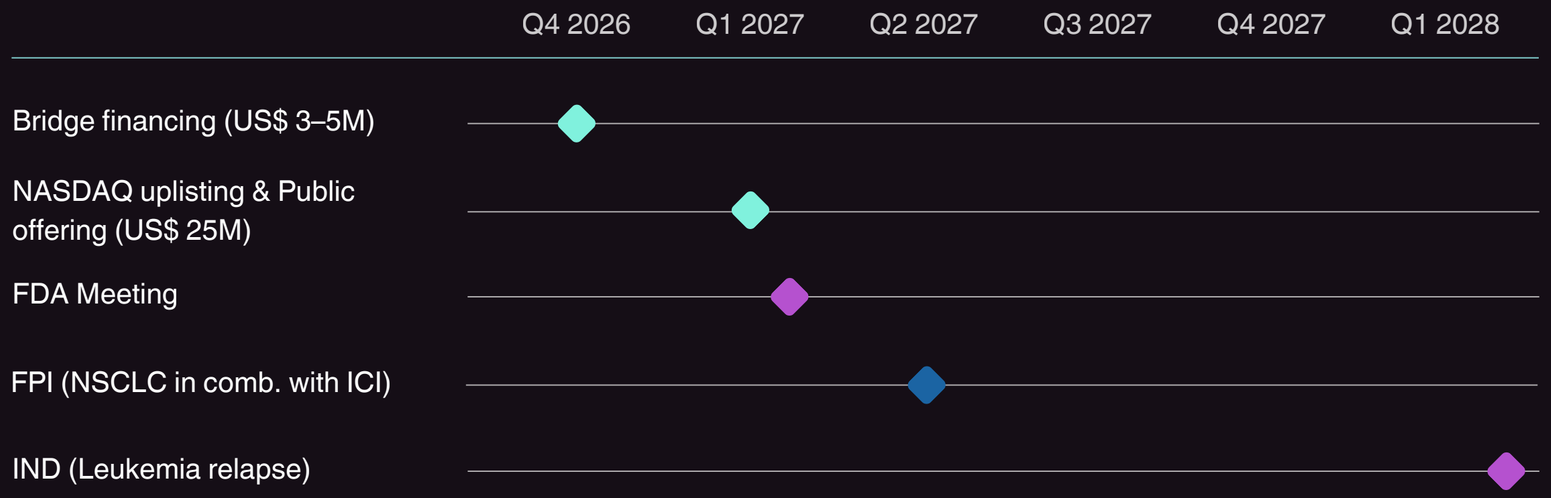
OUR STRATEGY

Innovating from strength to shape a near future where hard-to-treat cancers are *vincible*.

CANDIDATE	L-DOS47	LEUMUNA™	GEMCEDA™	C6 RDCs & ADCs
HARD-TO-TREAT CANCER	Non-small cell lung cancer (NSCLC)	Leukemia relapse	Advanced solid tumors	Solid tumors
HOW IT INNOVATES FROM STRENGTH	Synergistic efficacy with pembrolizumab (checkpoint inhibitor; standard of care)	Backed by clinical safety and efficacy data + FDA Orphan Designation	WHO Essential Medicine with oral bioavailability on par with IV (90%)	Latest state-of-the-art ADC technology and CEACAM6 know-how
HOW IT MOVES THE NEEDLE	Add ≥30% efficacy to checkpoint inhibitors	Long-term remission (2+ years) or cure	Significant increase in progression-free survival	Overcome resistance, maximize efficacy
STAGE OF DEVELOPMENT	Clinical-stage	Pre-IND	Pre-IND	Discovery

UPCOMING MILESTONES

Our ambitious plan on our priority projects over the next 18 months.



- Financial / Corporate Milestone
- L-DOS47 Milestone
- LEUMUNA Milestone

FPI: First Patient In.

EXPERT COLLABORATORS' OPINIONS

on Helix BioPharma's most advanced assets.

Professor Robert Gillies, Moffitt Cancer Center Vice-Chair Radiology, Director of Experimental Imaging Program & US Key Opinion Leader, **on L-DOS47**

"For years, we have proven that neutralizing the acidic tumor environment can prolong the life of mice. [...] However, our trials in the clinic have not been successful. We are excited to be able to use Helix's technology because it allows us to neutralize the acidic tumor environment directly and very precisely. We have high expectations that this will be an innovative approach to successfully treat cancer."

Professor Caius Radu, Departments of Molecular and Medical Pharmacology and Surgery, UCLA, California, US **on LEUMUNA**

"There is a good chance of recovery in patients. [...] It's effective in terms of inhibiting PNP, it's very effective in mice and patients, and given its mechanism of action could be used across a variety of malignancies including converting a cold tumor into one that could better respond to immunotherapy."

FORWARD-LOOKING STATEMENTS

This presentation document contains certain forward-looking statements and information (collectively, “forward-looking statements”) within the meaning of applicable securities laws. Forward-looking statements are statements and information that are not historical facts but instead include financial projections and estimates; statements regarding plans, goals, objectives, intentions and expectations with respect to Helix’s future business, operations, research and development, including the focus of Helix on its CEACAM6 platform generally and CEACAM6-AEC in particular, the anticipated timelines for the commencement or completion of certain activities, including enrolment of patients in Helix’s clinical trials, the expansion of the CEACAM6 platform into other compounds and indications and other information in future periods. Forward-looking statements, which may be identified by words including, without limitation, “expects”, “plans”, “will”, “intends”, “may”, “pending”, “objective”, “exploring”, “potential”, “projected”, “possible” and other similar expressions, are intended to provide information about management’s current plans and expectations regarding future operations.

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HELIX biopharma

Shaping a near future where today's hard-to-treat cancers are *vincible*.

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