New Directions in Cancer Therapy

HELIXBIOPHARMA

Investor Presentation

April 2023

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 DOS drug candidate generally and L-DOS47 in particular, the anticipated timelines for the commencement or completion of certain activities, including enrolment of patients in Helix's Phase I/II clinical trial for L-DOS47 in Poland, the expansion of the DOS47 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.

Although Helix believes that the expectations reflected in such forward-looking statements are reasonable, such statements involve risks and uncertainties that may cause actual results or events to differ materially from those anticipated and no assurance can be given that these expectations will be realized, and undue reliance should not be placed on such statements. Risk factors that could cause actual results or events to differ materially from the forward-looking statements include, without limitation: (i) the inherent uncertainty involved in scientific research and drug development, including with respect to costs and difficulties in predicting accurate timelines for the commencement or completion of certain activities; (ii) the risks associated with delay or inability to complete clinical trials successfully and the long lead-times and high costs associated with obtaining regulatory approval to market any product which may result from successful completion of such trials; (iii) need to secure additional financing on terms satisfactory to Helix or at all, including that the additional funding required in order to complete the proposed U.S. Phase I clinical trial will be obtained on terms satisfactory to Helix or at all; (iv) clinical trials that yield negative results, or results that do not justify future clinical development, including that Helix's ongoing Polish Phase I/II clinical trial for L-DOS47 and/or that Helix's proposed U.S. Phase I clinical trial will yield negative results; (v) Helix's clinical development plan for the proposed US Phase I clinical trial does not proceed in the manner or on the timelines anticipated by Helix or at all; and (vi) those risks and uncertainties affecting Helix as more fully described in Helix's most recent Annual Information Form, including under the headings "Forward-Looking Statements" and "Risk Factors", filed under Helix's profile on SEDAR at www.sedar.com (together, the "Helix Risk Factors"). Certain material factors and assumptions are applied in making the forward-looking statements, including, without limitation, that the Helix Risk Factors will not cause Helix's actual results or events to differ materially from the forward-looking statements. Helix.

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Executive Summary

- Helix BioPharma is developing a novel **first-in-class** anti-cancer therapy stemming from its proprietary technology platform
- Our lead Tumor Defence Breaker™ L-DOS47 is a unique **tumor microenvironment** modifying drug. It breaks the tumor defence against the innate (cellular) immune system by normalizing tumor acidification using a conjugate of a tumor specific antibody and urease - potentially allowing for better efficacy in **combination** with chemotherapy, checkpoint inhibitors and other mechanisms including CAR-T
- L-DOS47 has been used in **over 100 patients**, in mono-, and combo, treatments in NSCLC and PDAC demonstrating good tolerability and safety
- We have seen **promising data in a NSCLC trial** in combination with Pemetrexed/Carboplatin chemotherapy; a trial in pancreatic patients is underway
- Very recent promising preclinical data **combining L-DOS47 with PD1 inhibitor** (Checkpoint). Significantly **better tumor reduction** versus PD1 solo.
- The 2023 fund raising round of $10M will be used to finalise important preclinical experiments to secure the next significant value inflection point making the company attractive for partnering discussions

CORPORATE BRIEF

- Est. 1996, clinical-stage, biopharmaceutical company
- Listed/trades on the Toronto Stock Exchange (TSX): Helix BioPharma Corp. (“Helix”) / Ticker symbol – HBP
- Shares outstanding: around 200 M
- Share price: CAD 0.21 (04/09/2023)
- Market Capitalization: CAD 42 M
- Backed by high-net-worth investors
- Experienced Management team

MANAGEMENT TEAM

Jacek Antas, CEO
- Supervisory Board Chairman
- Over 25 years of experience in financial services/Board member for various companies

Gary Renshaw, MD, CMO
- Former CMO Zhejiang DTRM Biopharma
- Former oncology Director at Eisai

Hatem Kawar, CFO
- Experienced CFO with proven track record in managing financial business in a listed company

Advisors to the Board

Atul Deshpande, PhD MBA
- Experienced biotech entrepreneur, Commercial launch, fundraising and IPO experience for an IO company
- Former CEO, Immediate Therapeutics, Chief Strategist Harbour BioMed

Christof Boehler, PhD
- Biomedical scientist and experienced biotech entrepreneur
- Working with Big Pharma (Takeda) with a focus on drug delivery and oncology

BOARD OF DIRECTORS

Jacek Antas
CEO, Chair Board of Directors

Jerzy Leszczynski
Board Member

Christopher Maciejewski
Board Member

Malgorzata Laube
Board Member

ONCOLOGY REMAINS A SIGNIFICANT UNMET MEDICAL NEED

Lung Cancer in US

Estimated New Cases in 2022	236,740
% of All New Cancer Cases	12.3%
Estimated Deaths in 2022	130,180
% of All Cancer Deaths	21.4%

5-Year Relative Survival
22.9%
2012–2018

Colorectal Cancer in US

Estimated New Cases in 2022	151,030
% of All New Cancer Cases	7.9%
Estimated Deaths in 2022	52,580
% of All Cancer Deaths	8.6%

5-Year Relative Survival
65.1%
2012–2018

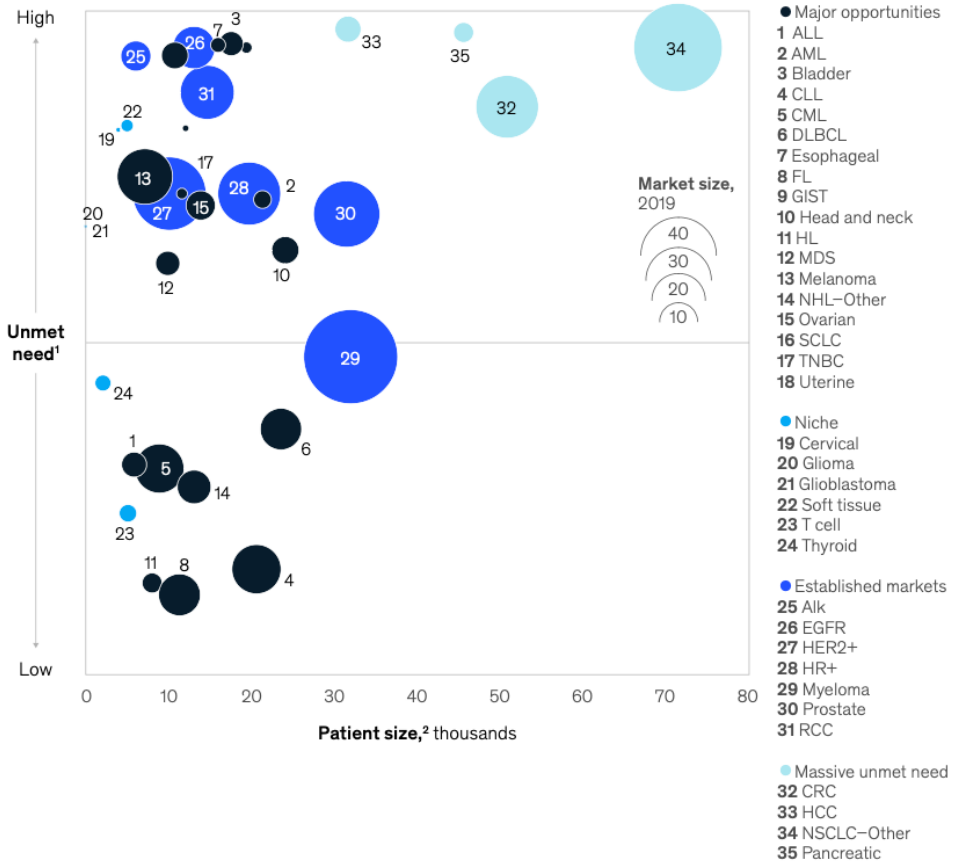
Head and Neck Cancer in US

Estimated New Cases in 2022	54,000
% of All New Cancer Cases	2.8%
Estimated Deaths in 2022	11,230
% of All Cancer Deaths	1.8%

5-Year Relative Survival
68.0%
2012–2018

From NCI SEER Program – Accessed 1/30/2023

Several tumor types impacting large populations have persistently high unmet need



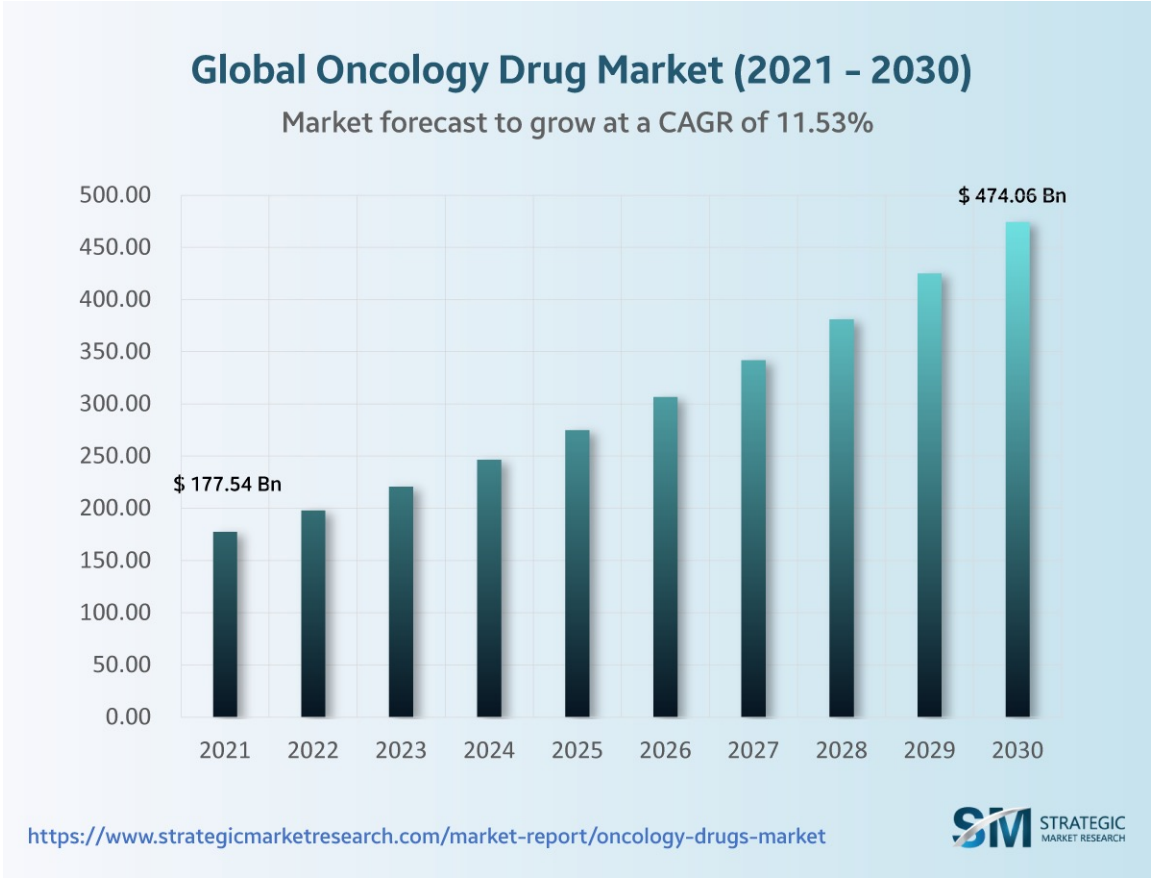
[1]Unmet need defined as one- minus five-year survival rate (overall for heme, metastatic for solid).
[2]Patient size calculated as annual incidence for heme, and larger of mortality and metastatic incidence for solid.

ESTIMATED IO MARKET BY 2030

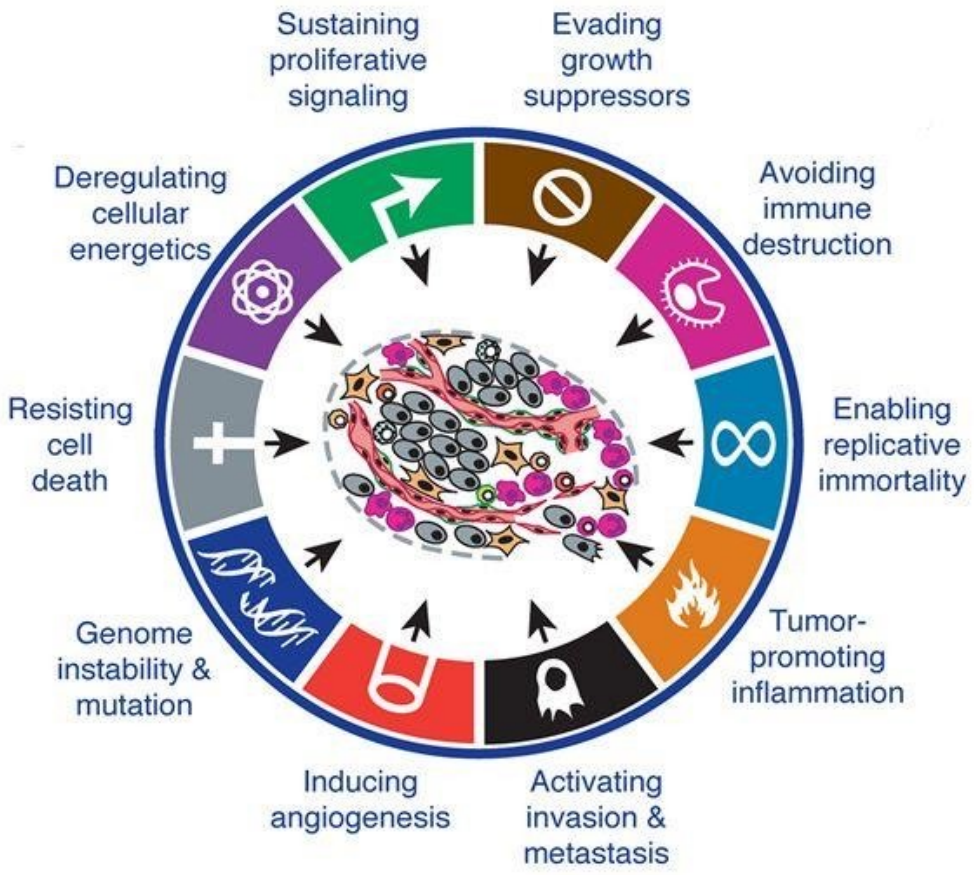
Growing aging populations, increasing obesity and changes in lifestyle including smoking and drinking has led to a significant increase in patients suffering from various kinds of cancers.

Increasing clinical and economic burden is putting a significant stress on our healthcare systems across the world.

Newer and more expensive therapies add to the toolkit to fight cancers thereby leading to a significant increase in market size over the next several years.



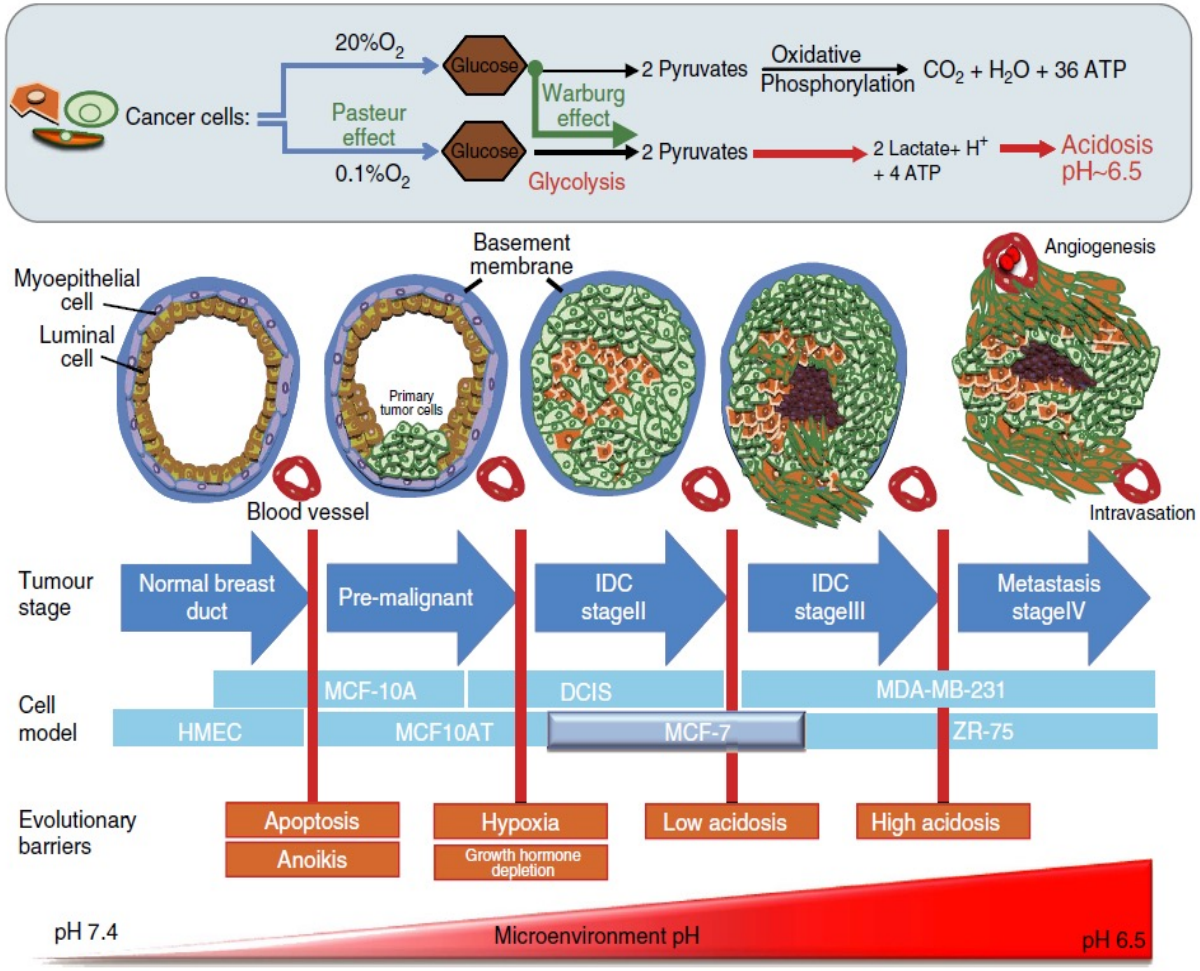
THE HALLMARKS OF CANCER



- The characteristics of cancer can be organized into multiple hallmarks or traits
- These hallmarks provide a framework to study cancer and to develop drugs
- **Targeted drugs** are developed against specific traits, but cancers often acquire resistance and escape
- Missing are therapeutics against an emerging cancer hallmark focused on **tumor acidity,** which serves a general **defense** for the tumor

Source: Cell 2011 144, 646-674

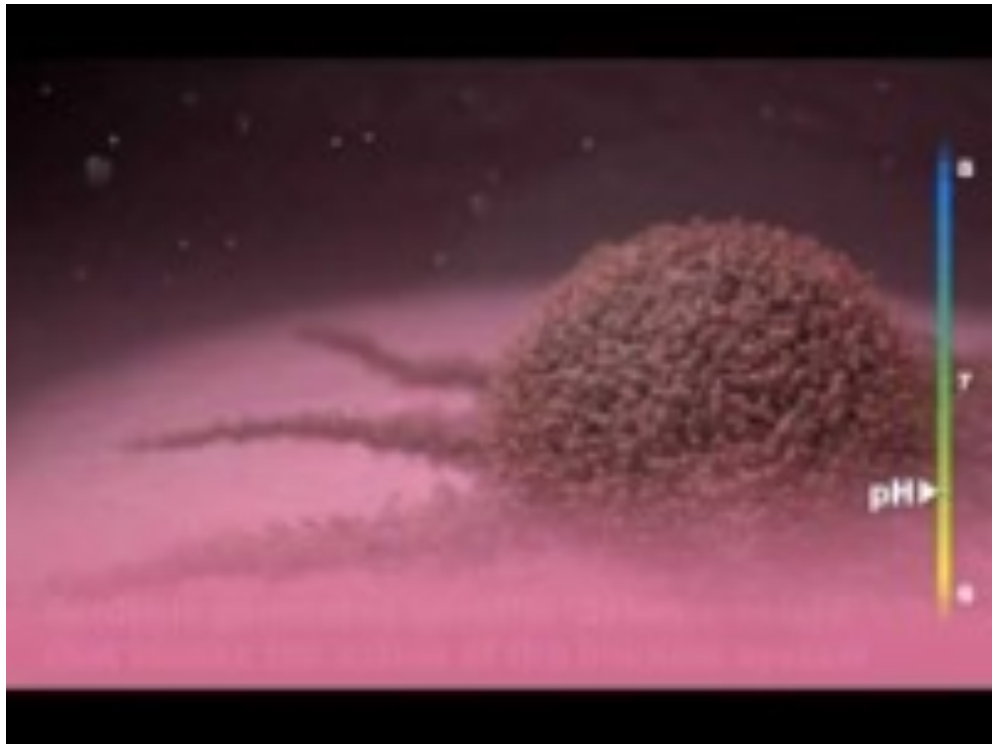
EFFECT OF ACIDOSIS ON TUMOR PROGRESSION



- Hypoxia, poor vasculature and increased flux of carbons through fermentative glycolysis leads to extracellular acidosis in solid tumors (Pasteur effect).
- Cancer cells can maintain the glycolytic phenotype even in the presence of oxygen (Warburg effect) causing further and constant acidification of the tumor microenvironment.
- Adaptation and development of resistance to acidosis is one of the key issues in cancer development and evolution that leads to a more aggressive phenotype.

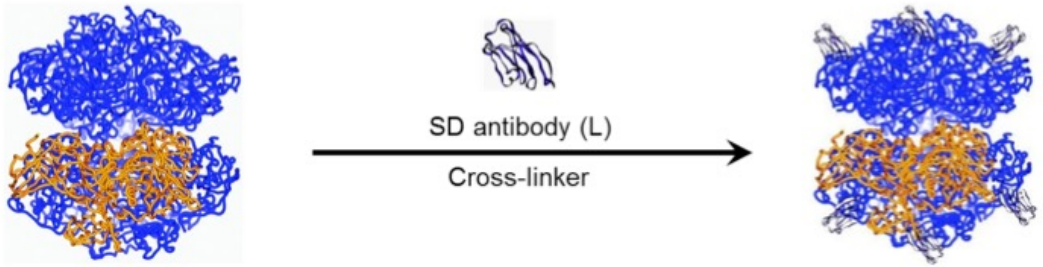
Source: Damaghi, M. et al. (2015). Nature Communications | 6:8752 | DOI: 10.1038/ncomms9752 |www.nature.com/naturecommunications

L-DOS47: A PLATFORM TECHNOLOGY TARGETING TUMOR MICROENVIRONMENT



1. Tumor acidity is an escape mechanism that cancer cells utilize to evade the anti-tumor immune response.
2. Tumor acidity has been shown to correlate with resistance to anti-cancer treatment and poor prognosis for cancer patients.
3. L-DOS47 is designed to reduce tumor acidity with a novel mechanism of action that is synergistic with other therapies
   i. It is an immune bioconjugate that binds to CEACAM6-expressing cancer cells
   ii. It converts urea into ammonia and raises pH: Acidity reversal may augment and repair immune function
   iii. L-DOS47 may improve uptake of weak-base chemotherapeutics
   iv. Preliminary data suggest that L-DOS47 can enhance efficacy of Anti-PD1 therapy
4. Favorable drug safety profile

L-DOS47: ANTI-CEACAM6 -UREASE BIOCONJUGATE



CEACAM6

- Glycosylated 90 kDa (286 aa) GPI-linked membrane protein
- Intercellular adhesion molecule forming homotypic and heterotypic bonds with CEACAM-1, -5 and -8
- Tumor antigen highly expressed on lung, colon, pancreatic and other cancer cells

Anti-CEACAM6 antibody: AFAIKL2

- Proprietary camelid single chain antibody
- As urease is a large protein, the small size of the camelid antibody (15 kDa) is beneficial – multiple antibodies conjugated to urease do not considerably increase total protein size

Conjugation of urease to a tumor-specific antibody allows targeted urease delivery by iv injection

Preclinical Studies

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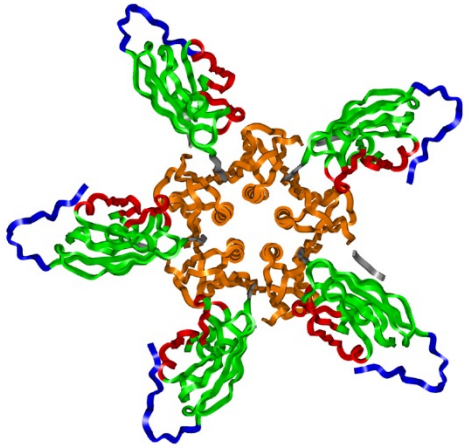
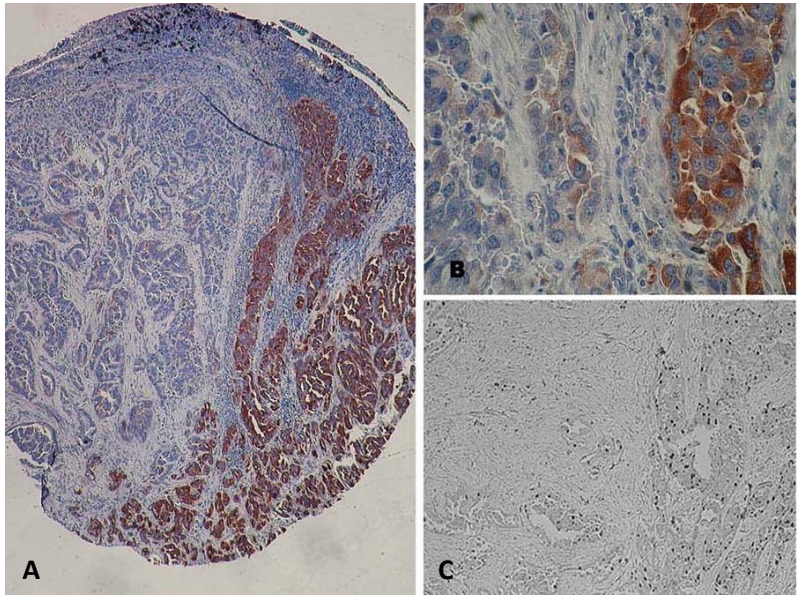
CEACAM6 IS OVEREXPRESSED ON MANY DIFFERENT TUMORS

ES1, a pentameric version of AFAIKL2, detects CEACAM6 on a range of tumors





Immunohistostaining of moderately differentiated lung adenocarcinoma. **A**: Staining with ES1. **B**: High magnification (X400) of an area in A. **C**: Staining with MIB1 (anti-Ki67) to indicate proliferation.

Table 2. A comparison of the immunoreactivity of ES1 with non-squamous large cell lung carcinomas and non-lung carcinomas

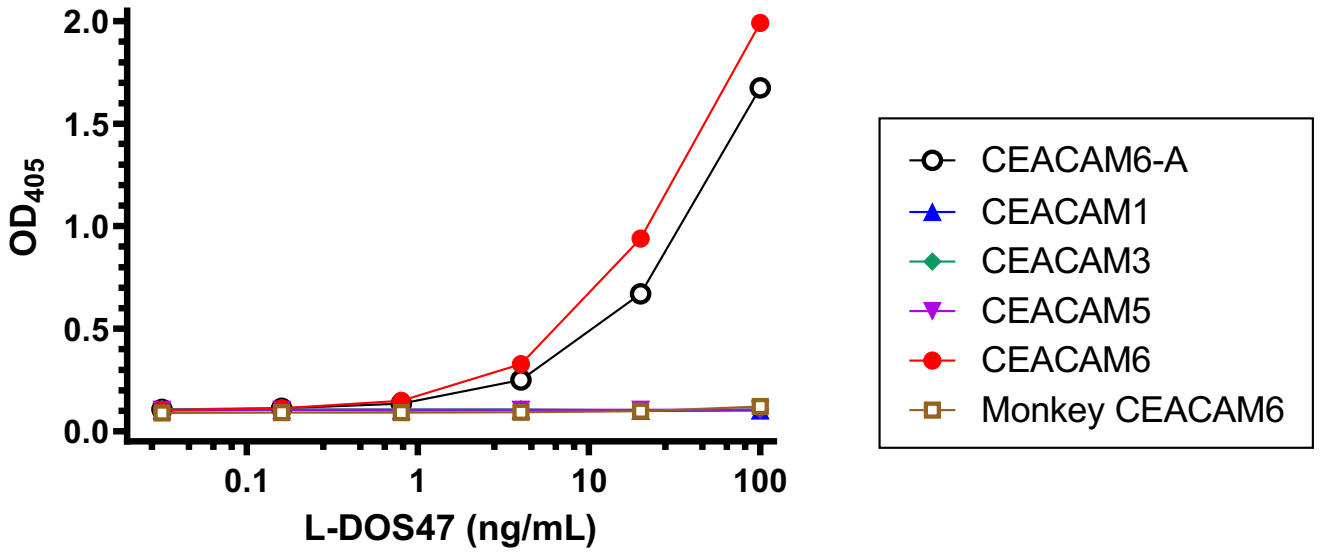
		Immunoreactivity	
Tissue	Total	Positive	Weak or negative
Non-squamous large cell carcinomas of the lung	35	34	1
Colonic adenocarcinoma	15	11	4
Breast carcinoma, urothelial carcinomas and non-colonic mucus-secreting adenocarcinomas*	38	18	20

*Pancreas, stomach, gallbladder, ovary (non-serous), urinary bladder and oesophagus.
The sensitivity of ES1 immunoreactivity for lung non-squamous and non-small cell carcinomas was 97% (34/35). The specificity was 45% (24/53). The positive predictive value was 54% (34/63).

Source: Modified from Mai, KT *et al. Histopathology*, 2006

L-DOS47 BINDS TO HUMAN CEACAM6 WITH HIGH SPECIFICITY

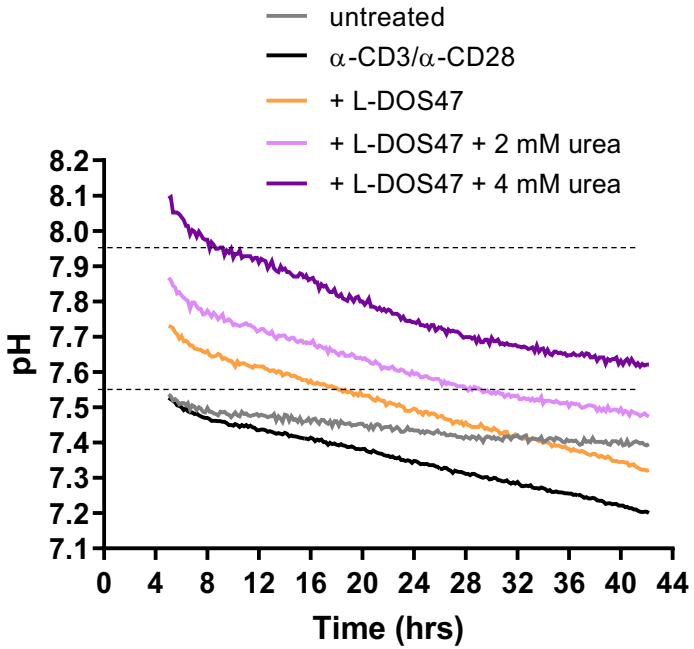
L-DOS47 is specific to human CEACAM6, not binding other human CEACAMs (1, 3, and 5) or cynomolgus monkey CEACAM6

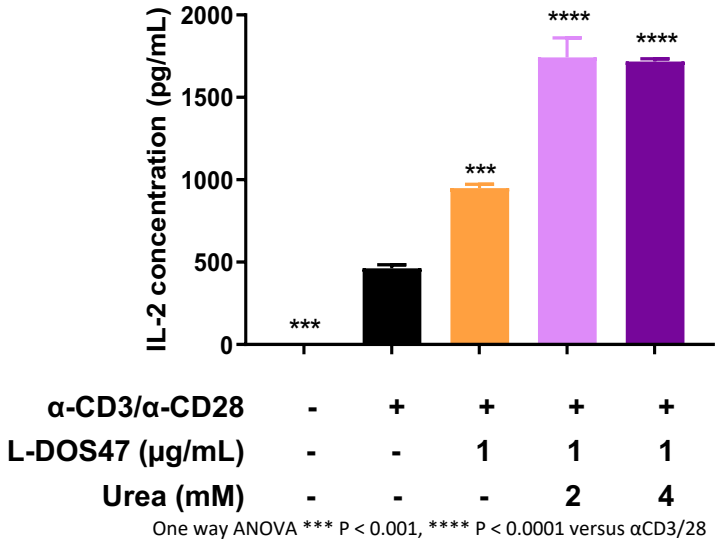


- ELISA binding assay using plates coated with CEACAM antigens (CEACAM6 = full length, CEACAM6A = peptide)
- incubated with L-DOS47, rabbit anti-urease antibody, alkaline phosphatase-conjugated anti-rabbit antibody, followed by substrate
- Signals detected on microplate reader correspond to presence of bound L-DOS47

L-DOS47 REDUCES ACIDITY THEREBY INCREASING IMMUNE CELL RESPONSES *IN VITRO*

A 0.4 unit increase in pH significantly enhances IL-2 secretion by CD8+ T cells





One way ANOVA *** P < 0.001, **** P < 0.0001 versus αCD3/28

- Purified CD8+ T cells activated with anti-CD3/anti-CD28 (to mimic antigen stimulation) for 3 days were continuously monitored *via* PreSens pH sensors
- L-DOS47 +/- its substrate, urea, were added at the indicated concentrations and incubated for 44 h
- Secreted IL-2 in supernatants was measured by ELISA

L-DOS47 DOES NOT ACTIVATE PRIMARY HUMAN OR MONKEY PBMCs *IN VITRO*

In the absence of its substrate, urea, L-DOS47 does not impact viability or induce proliferation in unstimulated PBMCs

Human and monkey PBMCs were treated *in vitro* with a range of L-DOS47 concentrations (1 – 50 µg/mL, corresponding to 1 – 50 mg/kg in human dosing) and proliferation was assessed by tritiated thymidine incorporation:

- human PBMCs did not proliferate in response to any L-DOS47 concentration tested
- viability was not impacted
- overall, the same was true for monkey PBMC except in one case (of six tested)

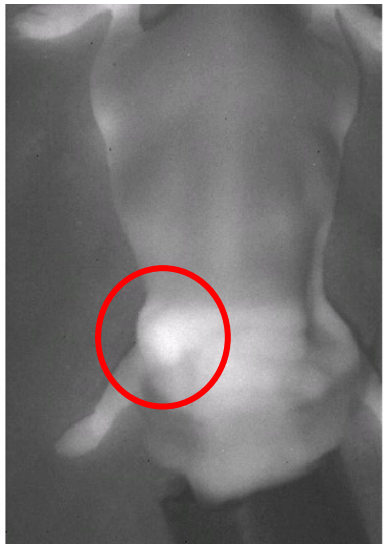
Similarly, L-DOS47 does not directly induce cytokine production by PBMCs *in vitro*

Human and monkey PBMCs were treated with 0.5 – 20 µg/well L-DOS47 and cytokine release into supernatants was quantified by Luminex assay:

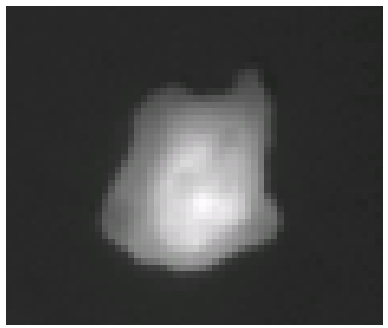
- Compared to negative controls, there was no significant induction of cytokines

L-DOS47 LOCALIZES TO CEACAM6-EXPRESSING TUMORS

8% of iv – injected L-DOS47 accumulated by 48 hours post-injection

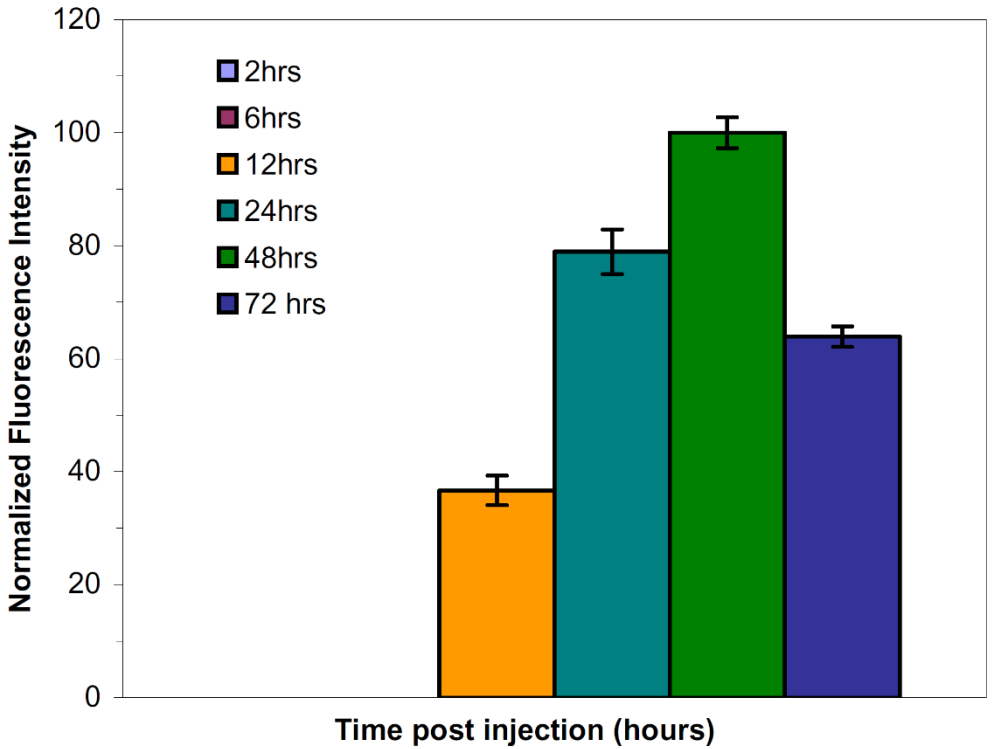


Fluorescence image of subcutaneous A549 lung tumor in nude mouse 72 hours after injection with Cy5.5-labelled L-DOS47



Fluorescence of extracted tumor (magnified)

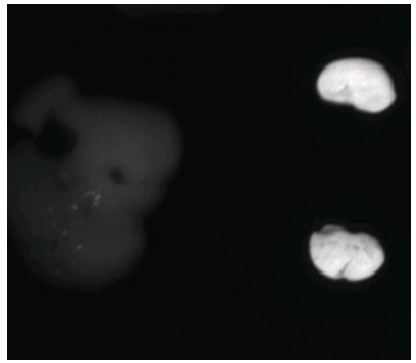
n = 4 mice sacrificed after imaging at each time point



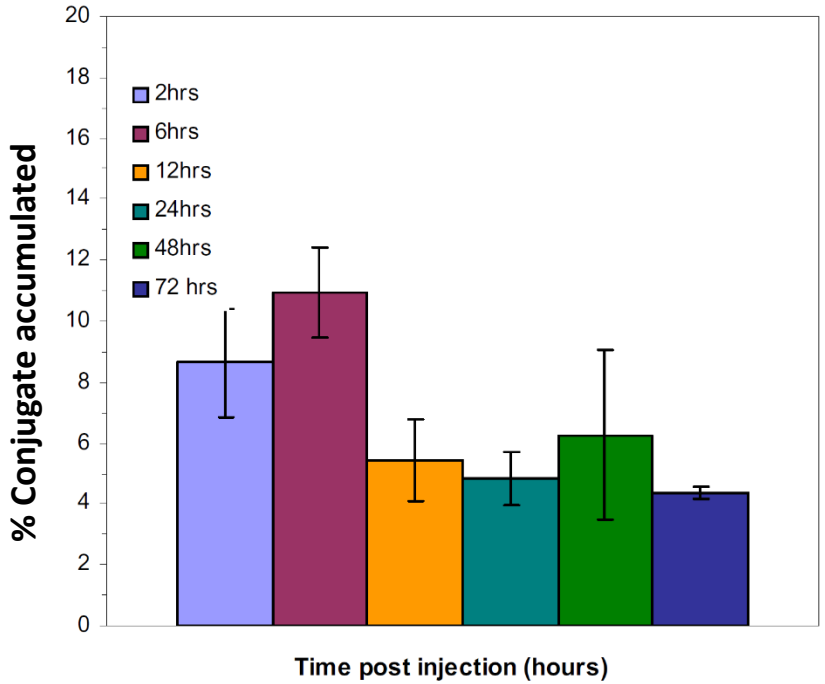
Mean normalized peak fluorescence intensity of tumors measured *in vivo* as a function of time; ~8% of iv-injected conjugate accumulated in tumors by 48hrs.

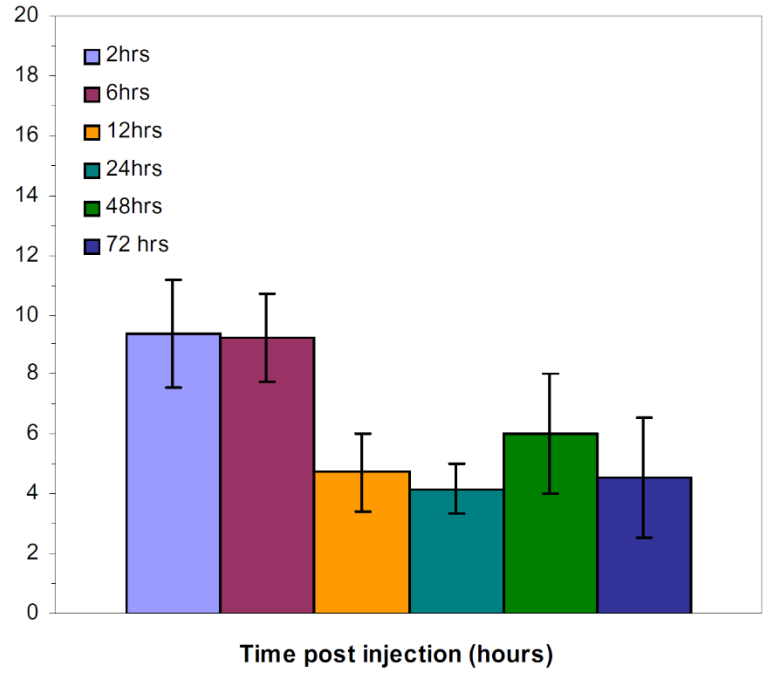
L-DOS47 RAPIDLY CLEARS LIVER AND KIDNEYS

Kidney accumulation of injected L-DOS47 Cy5.5 peaked at 18% at 2-6 hours and decreased thereafter



Ex vivo images of isolated liver (left) and kidneys (right) 72 hours post-injection



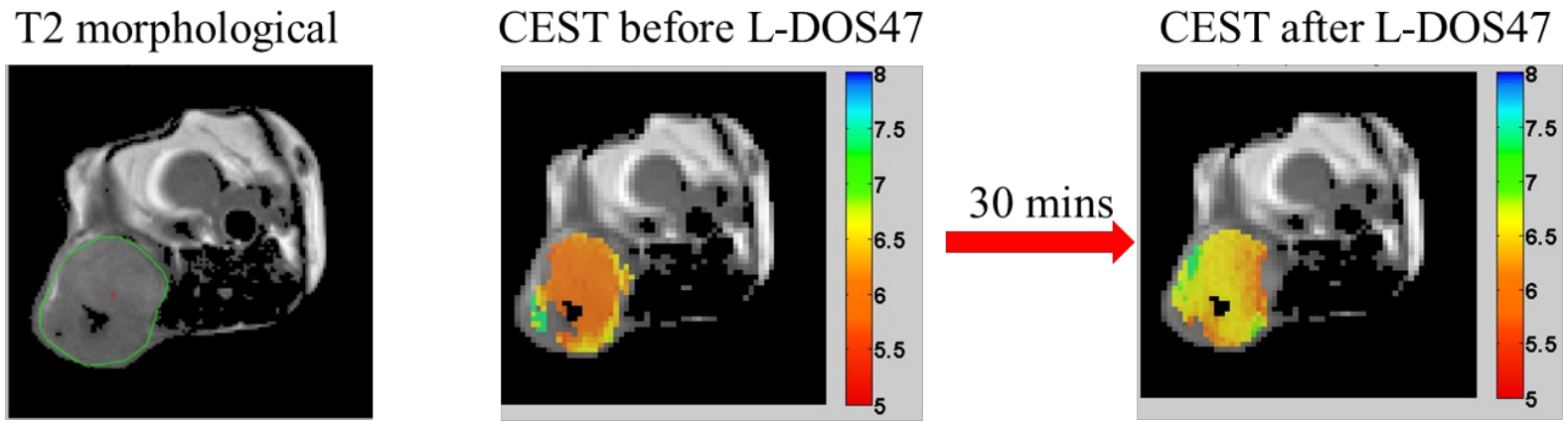


The percentage of total possible fluorescence was calculated for pooled data from the left (left) and right (right) kidneys harvested and imaged (from n = 4 mice per time point). No fluorescence was detected in blood, spleen, heart or lungs. Weak signals were detected in liver. No fluorescence was observed in any organ or tumor in mice injected with free dye.

L-DOS47 INCREASES TUMOR pH *IN VIVO*

CEST MRI reveals pH increase between pre-dose and 30min post-L-DOS47 administration

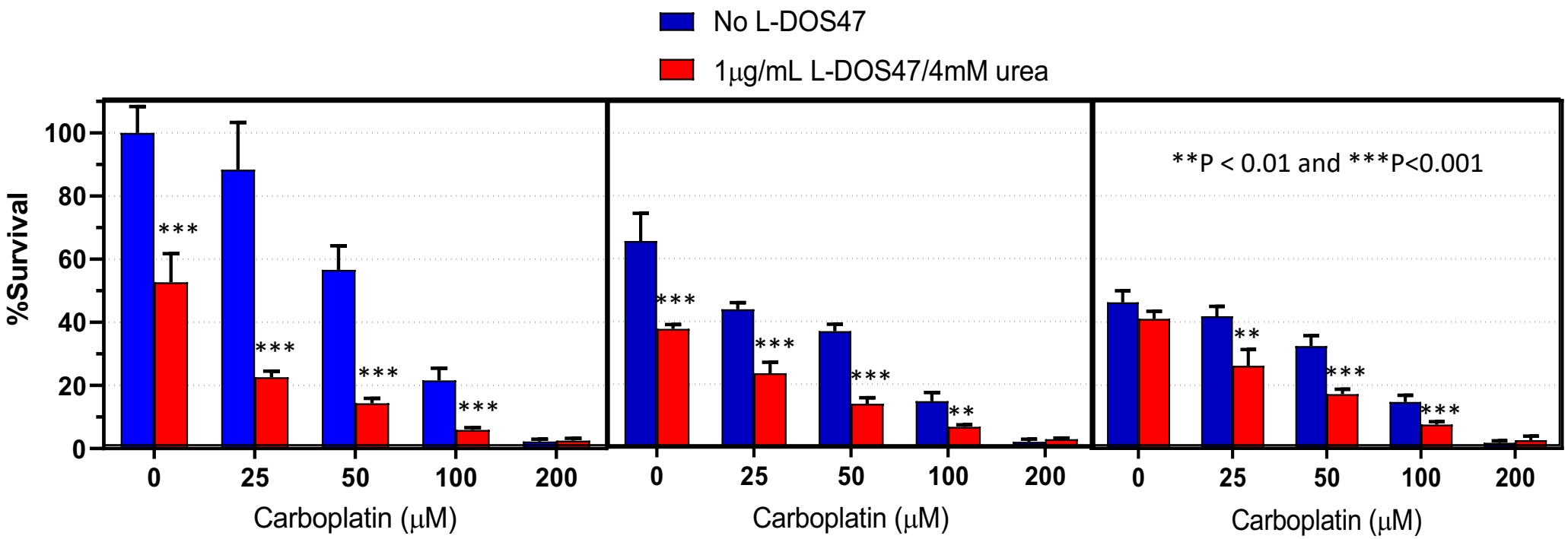
Proof of concept, single experiment



CEST MRI of Isovue 370 for pH imaging [1] of a Panc02 clone 38 SC tumor. (a) T2 weighted image, (b) CEST MRI before L-DOS47 injection, (c) ~30 minutes after 90 µg/kg L-DOS47 injection. The difference in mean pHs is 0.50 units. L-DOS47 was administered iv. Isovue 370 was administered SC, next to the tumor.

Additional CEST MRI revealing pH changes available under CDA

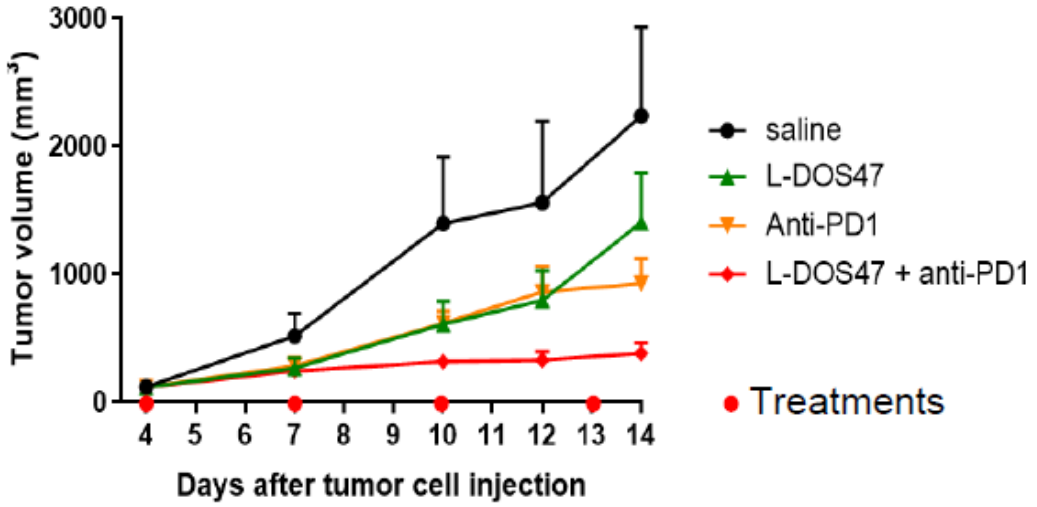
L-DOS47 ENHANCES CYTOTOXICITY OF CARBOPLATIN AND PEMETREXED



- A549 lung adenocarcinoma cells were treated with the indicated drugs for 72 hours after overnight seeding
- Viability was measured by resazurin assay
- In relative terms, 1μg/ml *in vitro* approximately corresponds to 1mg/kg in human dosing

L-DOS47 INHIBITS TUMOR GROWTH IN COMBINATION WITH ANTI-PD1

Tumor growth in a subcutaneous pancreatic tumor model



C57BL/6 mice (5 mice/group) were injected with CEACAM6-Panc02 cells subcutaneously in the right flank. Treatments started 4 days after tumor inoculation and all mice were sacrificed on day 15, after receiving 4 doses of drug(s). The combination of L-DOS47 and an anti-PD1 antibody controlled tumor growth. (Preliminary experiment)

- Anti-PD1 + L-DOS47 reduced Panc02 tumor growth compared to anti-PD1 alone
- Tumor volumes were measured by ultrasound
- **Preliminary experiment, significant orthotopic tumor data available under CDA**

ADDITIONAL ONGOING STUDIES

- *In vitro* and *in vivo* assessment of impacts of L-DOS47, pH changes and ammonium on primary human immune cells as well as on CEACAM6 and checkpoint marker expression on tumor cells
- Advanced imaging to confirm biodistribution of L-DOS47
- Assessment of tumor metabolism and acidity in refractory versus responsive settings
- Confirmatory studies to measure extracellular tumor pH changes in response to L-DOS47 in various preclinical cancer models
- Confirmatory *in vivo* efficacy of L-DOS47 + anti-PD1, testing both dosing orders in KPC961 orthotopic pancreatic cancer model
- Therapeutic efficacy of combination therapies in additional orthotopic cancer models

Clinical Studies

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Investor Presentation

March 2023

TUMOR DEFENCE BREAKER TECHNOLOGY PLATFORM

CLINICAL TRIALS		
L-DOS47 monotherapy NSCLC (clinical trial # NCT02340208)		
PRECLINICAL	PHASE 1	PHASE 2, stage 1
L-DOS47 combo PEM/CARBO NSCLC (clinical trial # NCT02309892)		
PRECLINICAL	PHASE 1	PHASE 2
L-DOS47 combo DOXO Pancreas (clinical trial # NCT04203641)		
PRECLINICAL	PHASE 1	PHASE 2

RESEARCH		
L-DOS47 combo Immune Checkpoints		
PRECLINICAL	PHASE 1	PHASE 2

A ROBUST CLINICAL STRATEGY TO ESTABLISH SAFETY AND EFFICACY OF L-DOS47 IN CANCER PATIENTS

Objective	Studies	Status	Outcomes
Safety and tolerability as a monotherapy	**LDOS002** Phase I/II Monotherapy in advanced non-small cell lung cancer (NSCLC)	Phase I and stage 1 of phase II complete	***L-DOS47 is safe and tolerated at all doses studied*** ***Limited efficacy observed – moved to combination studies***
Combo therapy with chemotherapy	**LDOS001** Phase I Combination with Pem/Carbo Phase I in advanced NSCLC	Published in J Thoracic Oncology - Clinical Research Reports (Piha-Paul, *et al*; Sept. 2022)	***L-DOS47 in combination with pemetrexed/carboplatin is well tolerated with promising anti-tumor activity***
Broaden utility and indications	**LDOS006** Phase Ib/II Combination with Doxorubicin in advanced pancreatic cancer	3 cohorts – 3, 6, 9 µg/Kg 20 patients dosed; 9 enrolled Amendment filed for higher dose at 13.55 µg/kg	***Dose escalation ongoing*** ***No L-DOS47-related DLTs seen to date***
Combining L-DOS47 with immunotherapy	Preclinical - Combination with immunotherapy in lung cancer or other indications	Planning	

LDOS002 STUDY DESIGN: MONOTHERAPY PHASE 1 & 2 IN NSCLC

Phase I:

- Dose escalation with modified Fibonacci, 3 + 3 design
- 16 dosing cohorts ranging from 0.12 to 13.55 µg/kg
- A dose-limiting toxicity (DLT) was defined as any NCI CTCAE v4.0, ≥ Grade 3 non-hematologic and any ≥ Grade 4 hematologic AE that is at least possibly related to L-DOS47 occurring ≤ 3 weeks after commencing L-DOS47 treatment
- L-DOS47 was administered once weekly over 14 days (Days 1 and 8) followed by 7 days rest (where one treatment cycle is 3 weeks)

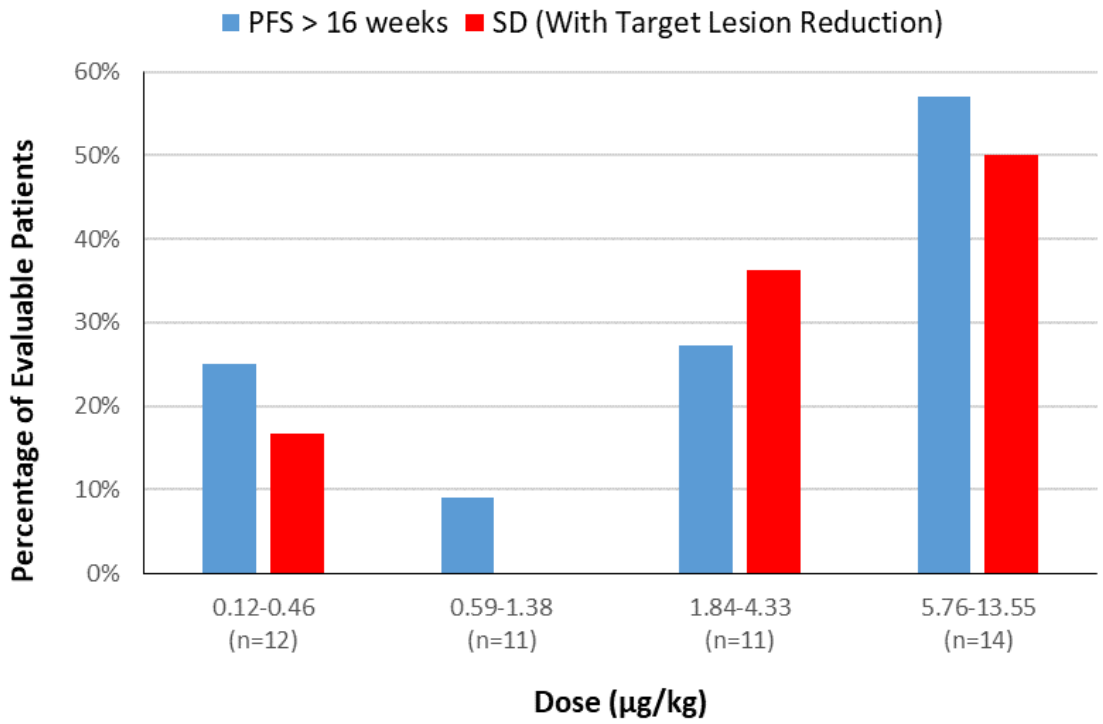
Phase II:

- Cohort 16 dose (13.55 µg/kg) selected for Phase II
- L-DOS47 dosing schedule was intensified from Phase I to twice weekly dosing over 14 days (Days 1, 4, 8, 11) followed by 7 days rest
- Utilized Simon's optimal two-stage study design where 17 evaluable patients were to be enrolled in the first stage of the Phase II component of the study; if ≥ 1 response(s) out of initial 17 evaluable patients, 22 additional evaluable patients were to be enrolled

LDOS002 RESULTS: A DOSE RESPONSE TREND WAS OBSERVED IN PFS AT 16 WEEKS WITH L-DOS47 MONOTHERAPY IN NSCLC

Phase I

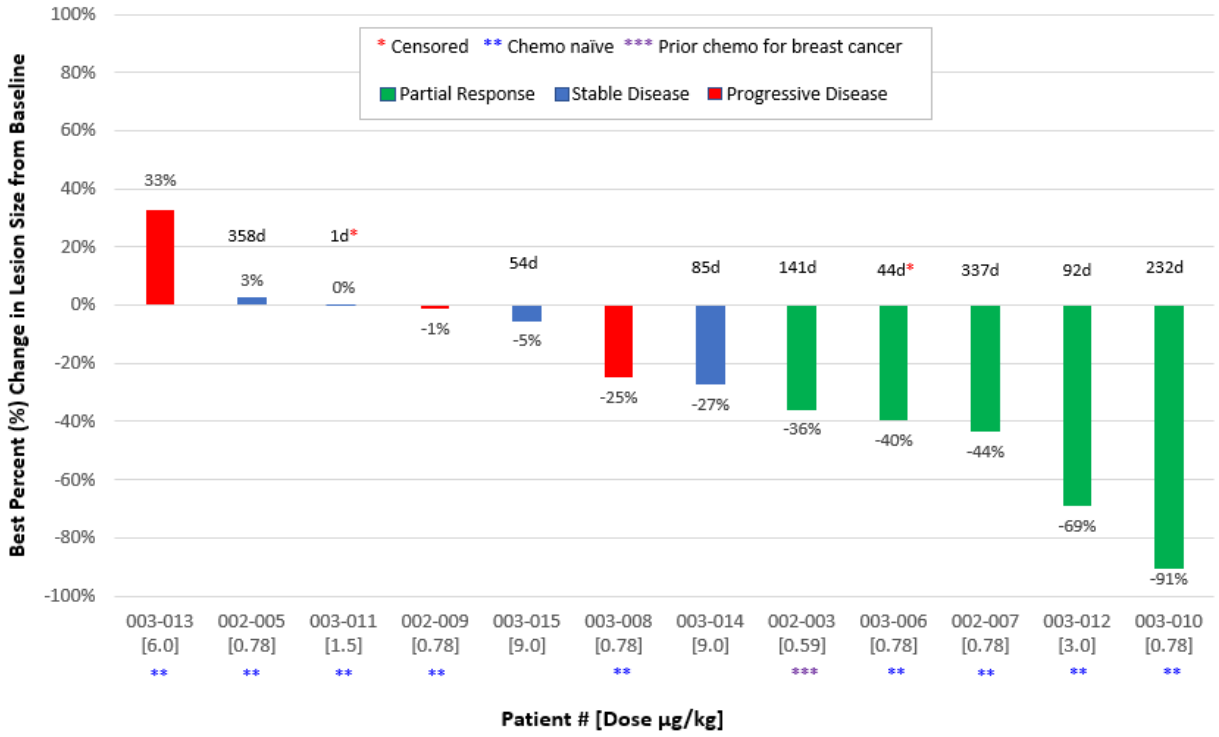
- L-DOS47 as a monotherapy is safe and well tolerated up to a dose of 13.55 µg/kg
- A dose response trend was observed when comparing the percentage of patients who were progression free at 16 weeks across dose ranges in Phase I
- A similar trend was observed when comparing the percentage of patients who had Stable Disease (as defined in RECIST v1.1) and had a reduction in target lesions
- While there were no confirmed partial responses, some tumor regression was observed in this late stage or heavily pre-treated patient population
- Phase I data indicated a clinical benefit was observed in non-squamous NSCLC patients



Phase II

- A total of 21 patients were exposed to a twice weekly dosing regimen at 13.55 µg/kg that remained relatively well tolerated
- Despite an intensified L-DOS47 monotherapy dosing regimen, evaluation of initial results did not yield the necessary partial or complete response to complete Stage 2
- Phase II 13.55 µg/kg was twice weekly, and the Phase I portion of 16 cohorts was weekly dosing

LDOS001 L-DOS47 PEMETREXED/CARBOPLATIN DOSE ESCALATION IN NSCLC



LDOS001 Phase I Trial Design

- Dose escalation study: 7 dosing cohorts
- Standard "3+3" design, with accelerated of "1+2" dose design for middle three cohorts (1.5, 3.0 and 6.0 µg/kg)
- Patients received up to four treatment cycles of combination treatment with L-DOS47 + pemetrexed/carboplatin
- Each treatment cycle was defined as 21 days: L-DOS47 dosed once weekly with pemetrexed/carboplatin dosed on Day 1 of each treatment cycle
- Patients had the option to continue to receive weekly L-DOS47 doses if they had not progressed following the four cycles of combination treatment and had not experienced unacceptable toxicity

Results

- Therapy well tolerated with **encouraging anti-tumor activity** in patients with recurrent or metastatic NSCLC at doses up to 9.0 µg/kg,
- Some patients continued once-weekly dosing of L-DOS47 alone up to 358 days
- 12 patients evaluable for efficacy, **5 patients (42%) with partial response** to treatment, **4 patients (33%) showed stable disease** and 3 patients (25%) had progressive disease. The objective response rate was 42% and the **overall clinical benefit rate was 75%.**

LDOS006: PHASE IB/II L-DOS47 DOXORUBICIN COMBINATION IN ADVANCED PANCREATIC CANCER

Phase Ib:

- Initial dose escalation phase applying a standard 3 + 3 algorithm, combining doxorubicin with L-DOS47
- Patients in each cohort receive weekly L-DOS47 (Days 1, 8, 15, 22) in combination with a fixed dose of 15 mg/m^2 doxorubicin (Days 2, 9, 16, 23) where one cycle is defined as 4 weeks
- A dose-limiting toxicity is defined as any occurrence within 28 days of commencing study regimen of following NCI CTCAE v5.0 events: Grade 4 neutropenia last > 5 days or Grade 3/4 neutropenia with fever and/or infection; Grade 4 thrombocytopenia (or Grade 3 with bleeding); Grade 3/4 non-hematologic (exception: Grade 3 mucositis)
- Patients who have not progressed may continue for up to 8 treatment cycles

Phase II:

- Additional 11 patients to be enrolled based on dose confirmed in Phase Ib portion of the study

Primary objective:

- To determine overall safety and tolerability of the treatment L-DOS47 in combination with doxorubicin
- To determine recommended Phase II dose of L-DOS47 in combination treatment with doxorubicin
- To assess preliminary anti-tumour activity

Secondary objectives:

- To assess the effect of L-DOS47 in combination with doxorubicin on tumour pH (as measured by SUV on FDG-PET)
- To determine the effect of combination treatment on pancreatic cancer biomarkers (change in CA19-9/CA-125)
- To assess the immunogenicity of L-DOS47 (presence of anti-L-DOS47 antibody)

LDOS006: PHASE IB/II L-DOS47 DOXORUBICIN COMBINATION IN ADVANCED PANCREATIC CANCER

Cohort 1
L-DOS47 3 µg/kg + Doxorubicin 20 mg/m²
Dec 2019

→

Cohort 1 (Amended)*
L-DOS47 3 µg/kg + Doxorubicin 15 mg/m²
Feb 2021

→

Cohort 2
L-DOS47 6 µg/kg + Doxorubicin 15 mg/m²
May 2022

→

Cohort 3
L-DOS47 9 µg/kg + Doxorubicin 15 mg/m²
Dec 2022

→

Cohort 4 (Planned Amendment)
L-DOS47 13.55 µg/kg + Doxorubicin 15 mg/m²
May 2023

→

Phase II
Dose TBD
Oct 2023

Phase Ib

Cohort	1	1 (Amended)*	2	3	4
Dose (µg/kg)	3	3	6	9	13.55
Minimum Cohort Size	3	3	3	3	3
Patients Dosed	6	8	4	2	-
Patients DLT Evaluable	3	6	3	2	-

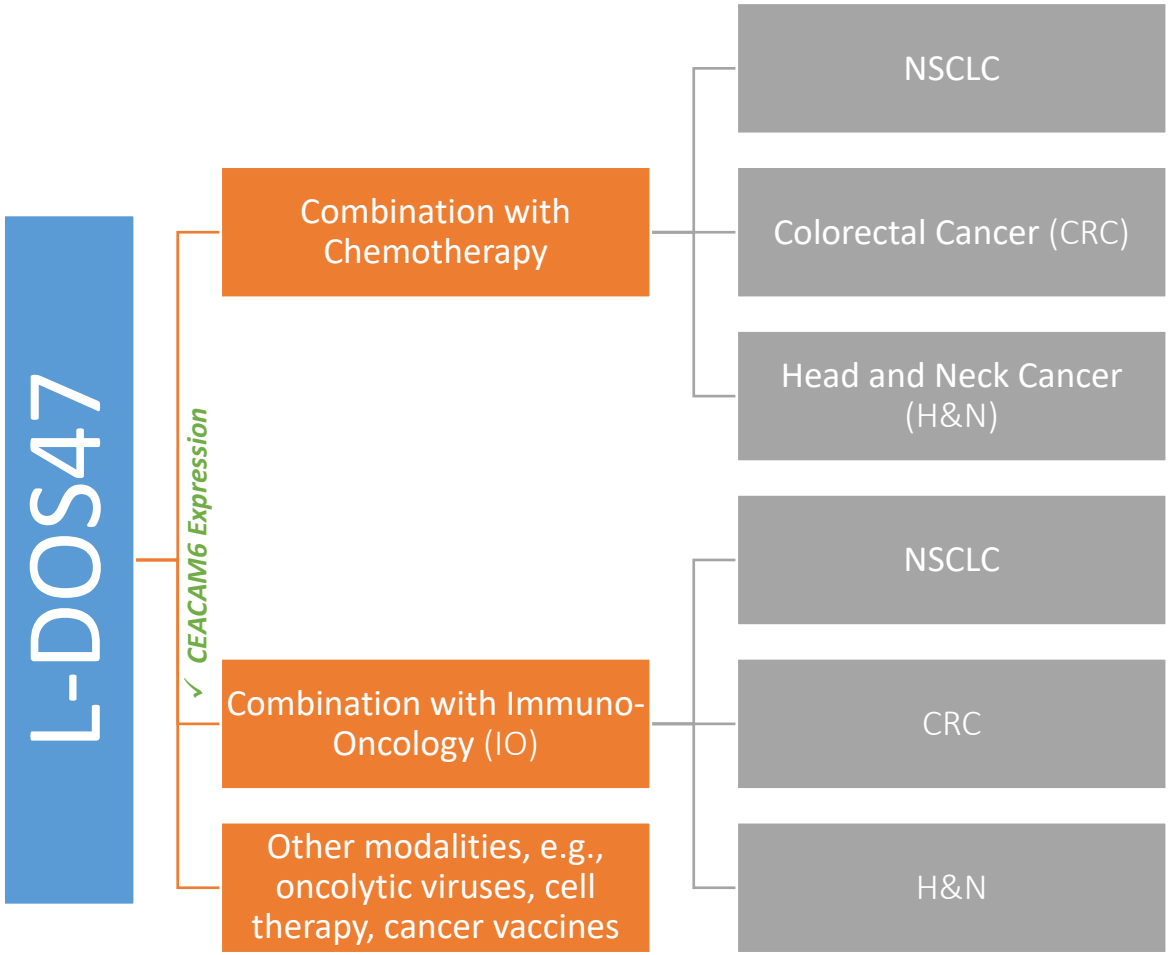
Phase II

Dose (µg/kg)	TBC
Target Enrolment	11
Patients Dosed	-

* Doxorubicin fixed dose was amended from 20 → 15 mg/m²

Future studies will be focused on MSI high and MSI moderate CRC

L-DOS47 PLATFORM: PORTFOLIO-IN-A-PRODUCT STRATEGY



L-DOS47 Platform

Combination with Chemotherapy

- ✓NSCLC – proof of concept with clinical data
- ➢ *CRC*
- ➢ *H&N*

Combination with IO Therapies

- ➢ *NSCLC*
- ➢ *CRC*
- ➢ *H&N*

Ongoing preclinical testing

Example companies

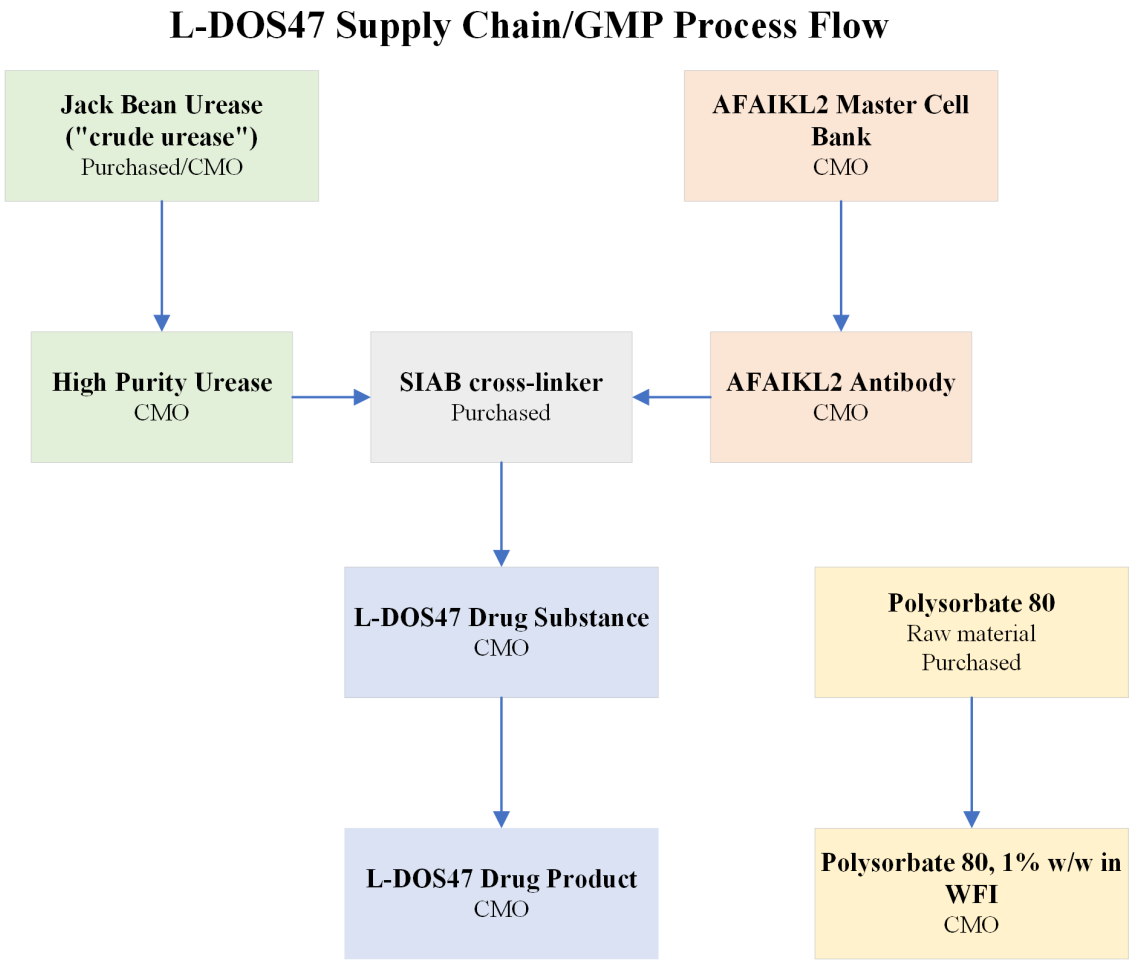
Lilly · Bristol Myers Squibb · Roche · Novartis · GSK · Pfizer · sanofi · Merck · Amgen · Johnson & Johnson

Manufacturing

HELIXBIOPHARMA

A WELL-ESTABLISHED SCALED-UP CMC PROCESS WILL ALLOW RAPID SUPPLY FOR CLINICAL TRIALS AND LAUNCH

L-DOS47 CMC Program



Current Status

- Three lots of L-DOS47 and 5 lots of Poly 80, 1% diluent have been used in clinical trials, all with **excellent stability**
  - Up to 8 years shelf life for L-DOS47
  - Up to 5 years shelf life for Poly 80, 1%
  - Established cGMP manufacturing process
- **Extensive QC** program for L-DOS47 and its components
  - Well-established specifications and reference standards
  - Qualified methods for identity, purity, potency, concentration, impurity profile and stability

Intellectual Property

HELIXBIOPHARMA

STRONG BARRIER TO ENTRY WITH IP

RESTORING FUNCTION TUMOR ACIDIFIED T CELLS	METHOD AND COMPOSITION FOR INHIBITING CANCER CELL GROWTH USING UREASE AND WEAKLY BASIC ANTI-CANCER COMPOUNDS	ANTIBODY-UREASE CONJUGATES FOR THERAPEUTIC PURPOSES		USE OF ANTIBODY-UREASE CONJUGATES FOR DIAGNOSTIC AND THERAPEUTIC PURPOSES	USE OF UREASE FOR INHIBITING CANCER CELL GROWTH (foundation technology)	
pH/urease direct effects on T cell function (Con't: Method to decrease expression of PD-L1 on cancer cell using urease) PCT/CA2017/051116	Use of composition to reduce amount of weakly basic anti-cancer compound to reduce tumor growth, unit dose of 10-50 units/mL urease & an anti-tumor antigen antibody to enhance the delivery of the urease to tumor. unit dose reduces the amount of said weakly basic anti-cancer compound 2-5-fold lower than without urease.	sdAb:AFAIKL2 urease conjugate (CEACAM6) optimized with novel conjugation ratios (3-12) PCT/IB2016/050342		2.5 120kDa Abs conjugated to urease enzyme, multiple points of conjugation on the antibody PCT/CA2014/050334	Pharmaceutical composition for inhibiting growth of cancer cells, comprising urease enzyme, and chemical entity effective to enhance the delivery of the enzyme to cancer cells. PCT/CA2003/001061	
U.S. 10,640,806 *U.S. 16/847,490 *CA 3,045,327 *EP 3515473 *CN 110011891	CA 2,493,282	U.S. 15/545,549 CA 2,973,538 AU 2016210551 EP 3261678 (validated in CH, DE, FR, GB, IT, NL, SE, and ES)	IN 367556 IL 253549 JP 6876618 SK 10-2318994 PL 238187	U.S. 10,316,311 AU 2014252666 CA 2,908,475 *EP 2984170	U.S. 7,211,250 U.S. 7,264,800 CA 2,492,472 EP 1530482+ (validated 30 countries) EP 2324846 (DE, FR,UK)	IN 245306 & 293956 JP 5850561 SK 10-1352826 NZ 538284 PL 217626 IL 166249 NO 336811
** Patent term expires Sept 22, 2037 (if all required annuities paid)	** Patent term expires Jan 31, 2025 (if all required annuities paid)	** Patent term expires January 22, 2036 (if all required annuities paid)		** Patent term expires April 3, 2034 (if all required annuities paid)	** Patent term expires July 16, 2023 (if all required annuities paid)	

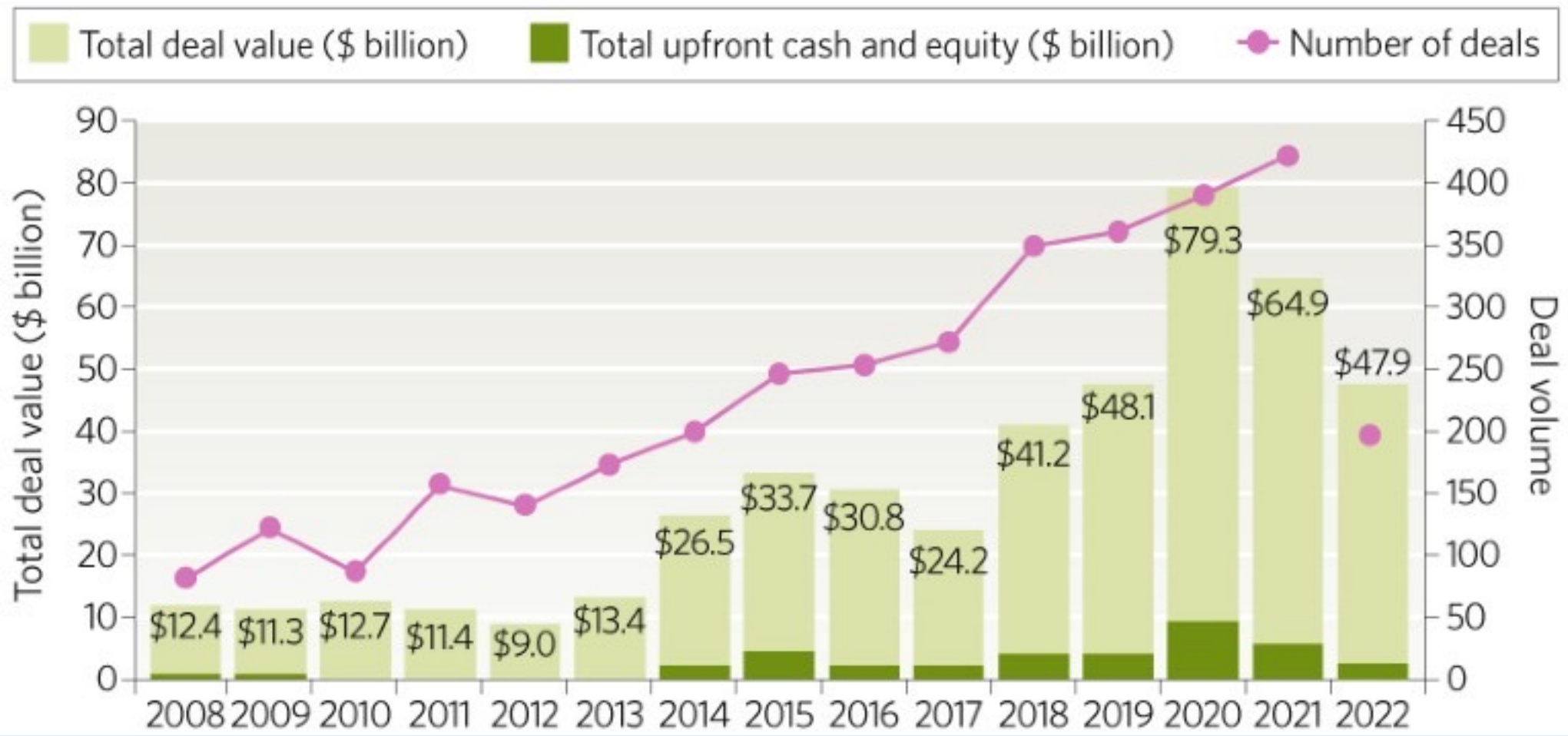
Business Development

HELIXBIOPHARMA

Investor Presentation

March 2023

R&D PARTNERSHIPS IN ONCOLOGY



R&D partnerships in oncology. Source: DealForma database. Financials based on disclosed figures as of 2 Aug 2022.

EXAMPLE OF TARGETS COMPANIES THAT COULD HAVE INTEREST IN L-DOS47

- Ongoing outreach to these and several other companies
- Interest to use LDOS47 in combination with their assets
- Could be of interest beyond current IO therapies to their growing portfolio
- In combination with newer modalities like mRNA, oncolytic vaccines among others

EXAMPLE COMPS FOR HELIX BIOPHARMA

Licensor and licensee	Total deal value ($ million), date	Description
Cullinan Oncology and Harbour BioMed	$588 ($25M upfront; $148M development milestones, $415 sales based tiered royalties) 14 Feb 2022	**Cullinan Oncology Licenses U.S. Rights to the First Clinical-Stage B7H4 x 4-1BB Bispecific Immune Activator from Harbour BioMed** Under the agreement, Cullinan Oncology will pay Harbour BioMed an upfront license fee of $25 million at closing for the exclusive right to develop and commercialize CLN-418/HBM7008 in the U.S. Harbour BioMed will be eligible to receive up to $148M in development and regulatory milestones plus up to an additional $415M in sales-based milestones as well as tiered royalties up to high teens on potential U.S. commercial sales.
Astrazeneca and Harbour BioMed	$350 ($25M upfront; $325M development milestones, sales based tiered royalties) 7 April 2022	**Harbour BioMed Announces Global Out-License Agreement with AstraZeneca for CLDN18.2xCD3 Bispecific Antibody HBM7022** Pursuant to the license agreement and subject to the terms and conditions thereof, HBM shall receive an upfront payment of US$25 million with the potential for additional payments up to US$325 million pending achievement of certain development, regulatory and commercial milestones. HBM is also eligible to receive tiered royalties on net sales.
Astrazeneca and Neogene Therapeutics	$320 ($200 upfront; $120 milestone based please royalties)	**AstraZeneca to acquire Neogene Therapeutics, accelerating ambition in Oncology cell therapy** AstraZeneca will acquire all outstanding equity of Neogene for a total consideration of up to $320m, on a cash and debt free basis. This will include an initial payment of $200m on deal closing, and a further up to $120m in both contingent milestones-based and non-contingent consideration.
Merck and Imago Biosciences	$1,350 (Terms not disclosed) November 21, 2022	**Merck to Acquire Imago BioSciences, Inc.** Merck, through a subsidiary, will acquire Imago for $36.00 per share in cash for an approximate total equity value of $1.35 billion. *Multiple assets in pipeline.*

USE OF THE PROCEEDS: $10M TILL DEC 2024

Pre-clinical Studies with Moffitt and Tubingen University - $3M

- New collaboration with University Hospital Tubingen to assess therapeutic responses of L-DOS47 in several cancer models expressing CEACAM6, with advanced preclinical metabolic imaging
- Ongoing collaboration with Moffitt Cancer Center, Tampa to study the synergistic effect of L-DOS47 in combination with checkpoint inhibitors in models of various tumor types

Ongoing Clinical Trial - LDOS006 Pancreatic Study - $4M

- An open-label, single arm study that includes an initial three cohort dose escalation phase with 3, 6 and 9 µg/kg of L-DOS47 in combination with doxorubicin

General Administration - $3M

- Operational Expenses for HBP

SUMMARY

1. **Current standards of care,** including checkpoint inhibitors, are **limited** by the efficacy in addressing cancers
2. Helix is developing novel anti-cancer therapies stemming from its proprietary technology platforms that could help address these efficacy challenges turning it into a significant **multi-pronged business opportunity** to potentially partner with different pharma companies
3. **L-DOS47**
   a) Unique tumor microenvironment immuno-conjugate drug
   b) proven safe and tolerable in a monotherapy lung cancer study
   c) gained additional clinical data when combined with chemo in lung cancer
   d) in clinical development for both lung and pancreatic cancer
4. Additional **clinical and pre-clinical milestones are expected in 2023** that will augment partnership discussions with pharma partners

Thank You!