



Transforming cancer treatment with Protein Phosphatase 2A inhibitors

Unveiling the first of a novel class of therapeutic agents

Forward looking statements

This information packet contains certain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, and Section 21E of the Securities Exchange Act of 1934. For example, statements regarding the Company's financial position, business strategy and other plans and objectives for future operations, and assumptions and predictions about future activities, including the continuing development of proprietary compounds, the planning, funding, coordination and potential results of clinical trials, the patent and legal costs to protect and maintain the Company's intellectual property worldwide, and the Company's ability to obtain and maintain compliance with Nasdaq's continued listing requirements, are all forward-looking statements. These statements are generally accompanied by words such as "intend," "anticipate," "believe," "estimate," "potential(ly)," "continue," "forecast," "predict," "plan," "may," "will," "could," "would," "should," "expect" or the negative of such terms or other comparable terminology.

The Company believes that the assumptions and expectations reflected in such forward-looking statements are reasonable, based on information available to it on the date hereof, but the Company cannot provide assurances that these assumptions and expectations will prove to have been correct or that the Company will take any action that the Company may presently be planning. However, these forward-looking statements are inherently subject to known and unknown risks and uncertainties. Actual results or experience may differ materially from those expected or anticipated in the forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, regulatory policies, available cash, research results, competition from other similar businesses, and market and general economic factors. This discussion should be read in conjunction with the Company's filings with the United States Securities and Exchange Commission at www.sec.gov.

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Immunotherapy: Great potential, many challenges

Broad Applicability

Applicable to different tumor types and stages.

Limited Efficacy

Intrinsic and acquired resistance to therapy limits its impact.

Safety Risks

Toxicity limits treatment dosage and duration, affecting efficacy.

Our unique approach: enhance existing therapies with PP2A inhibitors

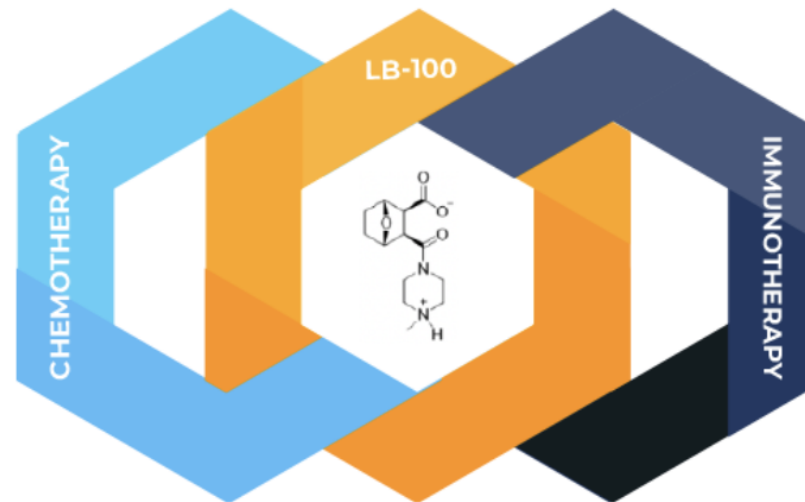
Pre-Clinical Evidence: LB-100 is a first-in-class enhancer of immunotherapy

CHEMOTHERAPY

+ LB-100

Enhanced chemotherapy efficacy

- Stimulates cell cycle
- Inhibits DNA repair



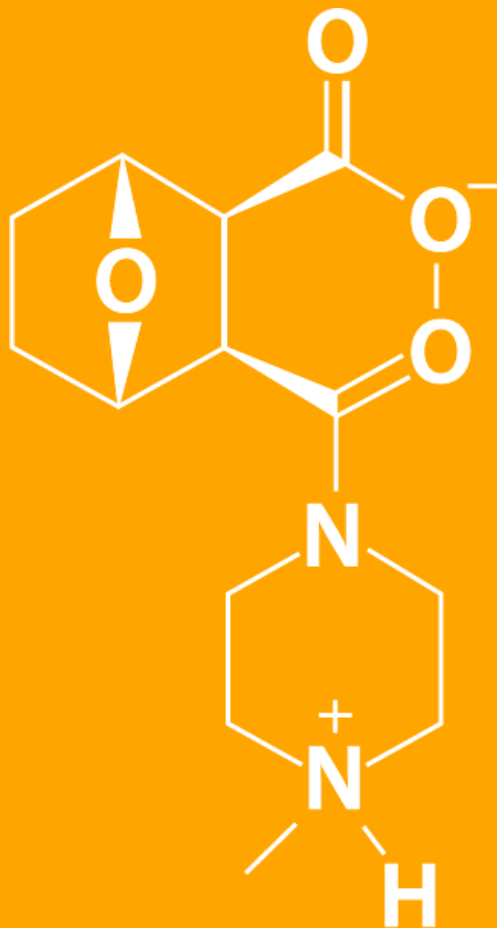
IMMUNOTHERAPY

+ LB-100

Enhanced immunotherapy efficacy

- Enhances T cell proliferation
- Increases release of cytokines
- Promotes production of neoantigens

LB-100



LB-100 is the first PP2A-inhibitor with a promising safety profile

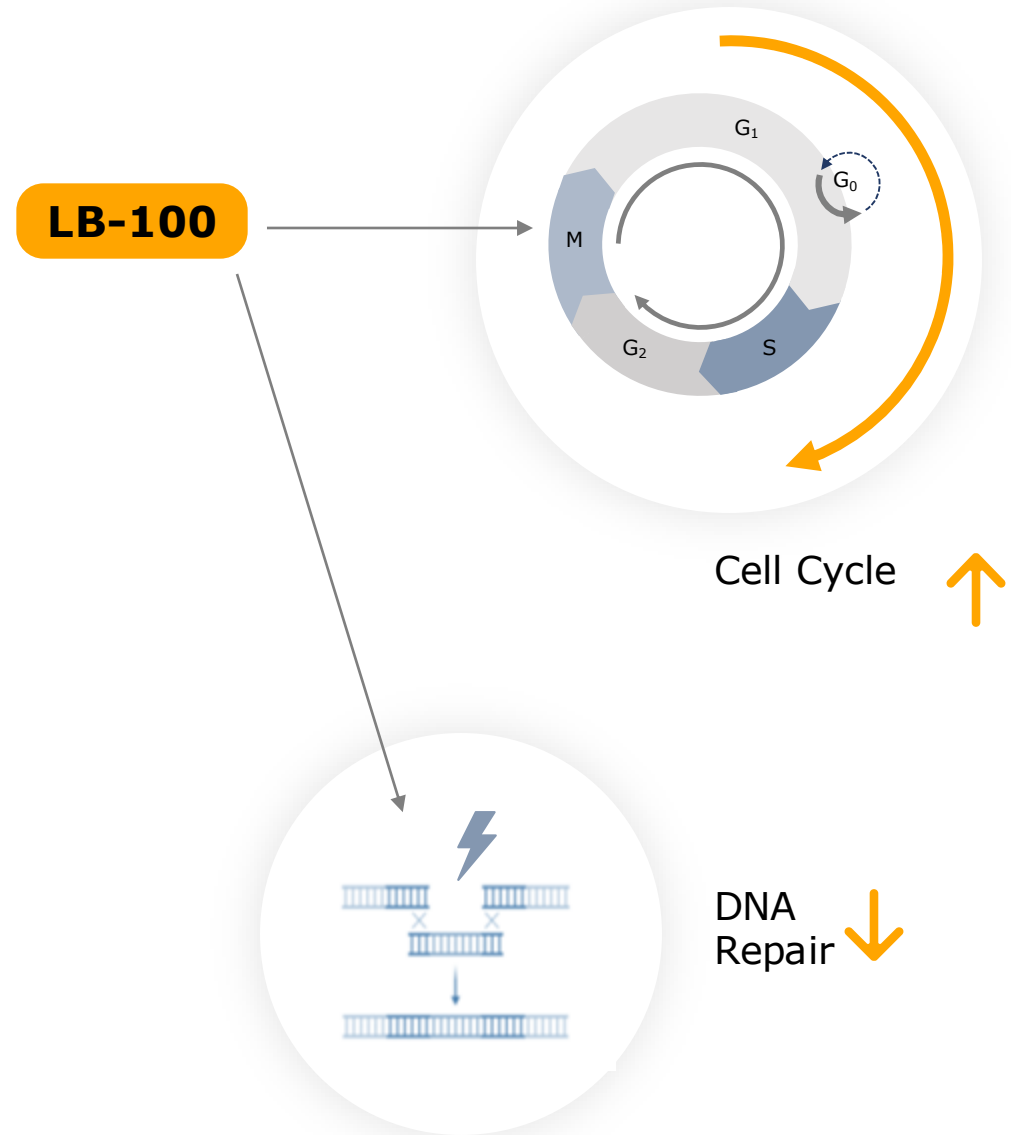
LB-100 is a small molecule inhibitor of the PP2A phosphatase, a critical enzyme involved in multiple cellular functions.

- Demonstrated safety in 2 phase 1 clinical trials *NCT01837667 and NCT03027388*
- Documented anti-cancer activity in 25+ publications
- Convenient IV delivery and cost-effective manufacturing
- Good Manufacturing Practice production in place
- FDA: Investigational New Drug (IND) status
- European Medicine Agency: Investigational Medicinal Product Dossier approval Europe in 2022

LB-100: Lethal Activation

LB-100 stimulates cell cycle and inhibits DNA repair

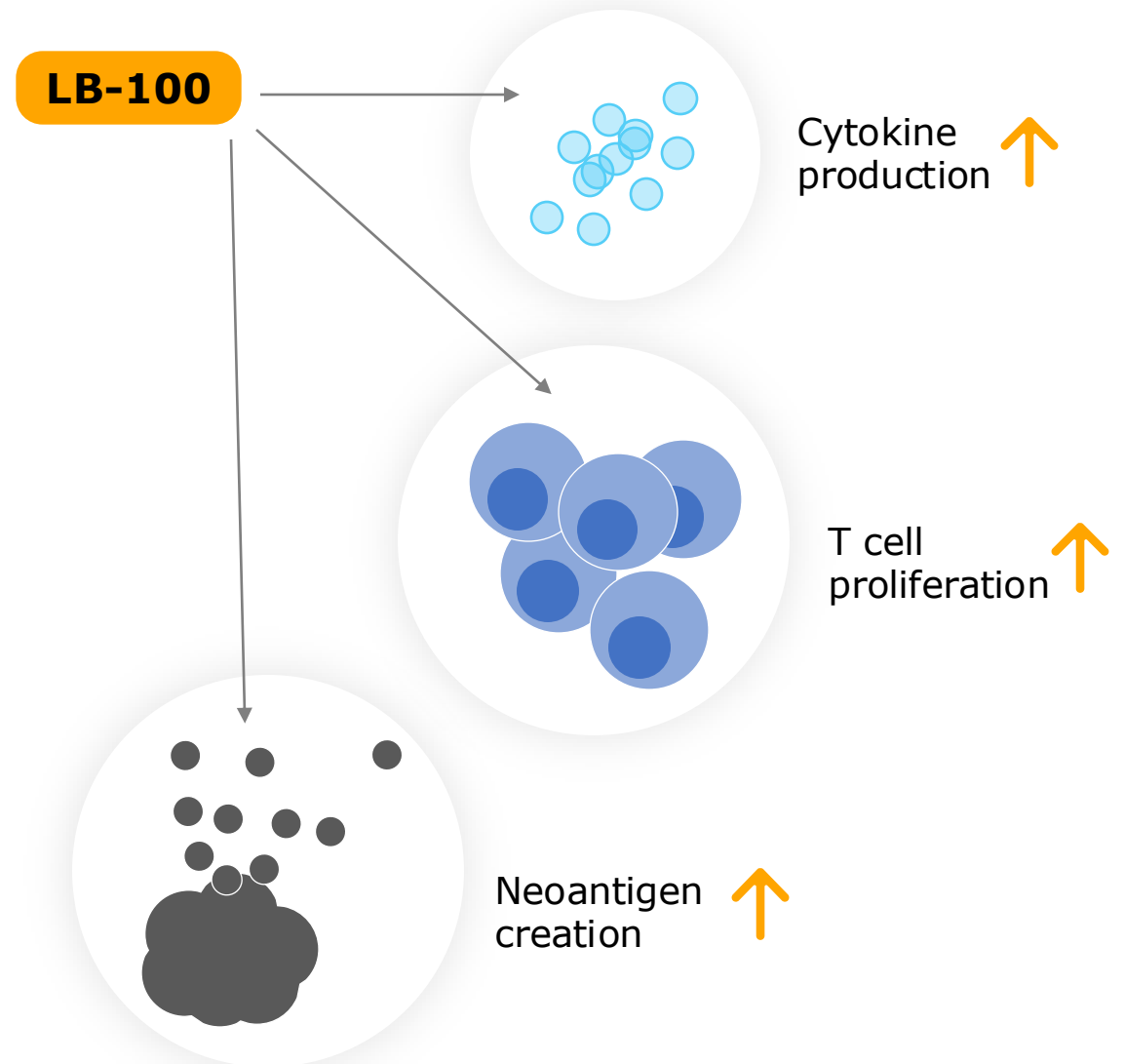
This renders cancer cells more susceptible to chemotherapy agents, thus enhancing the treatment's effectiveness.



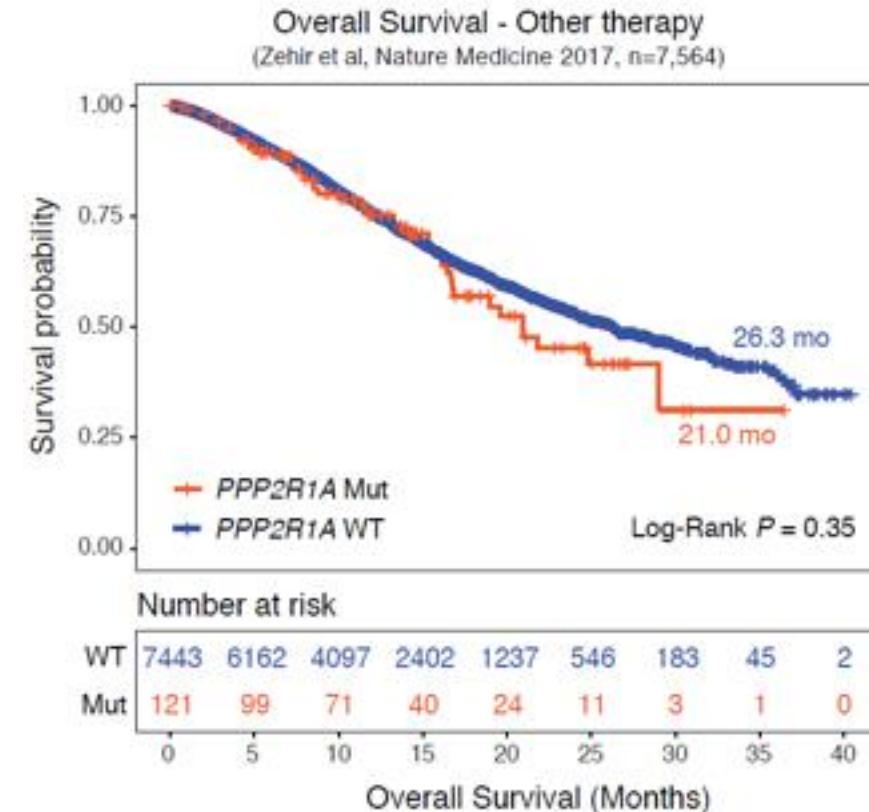
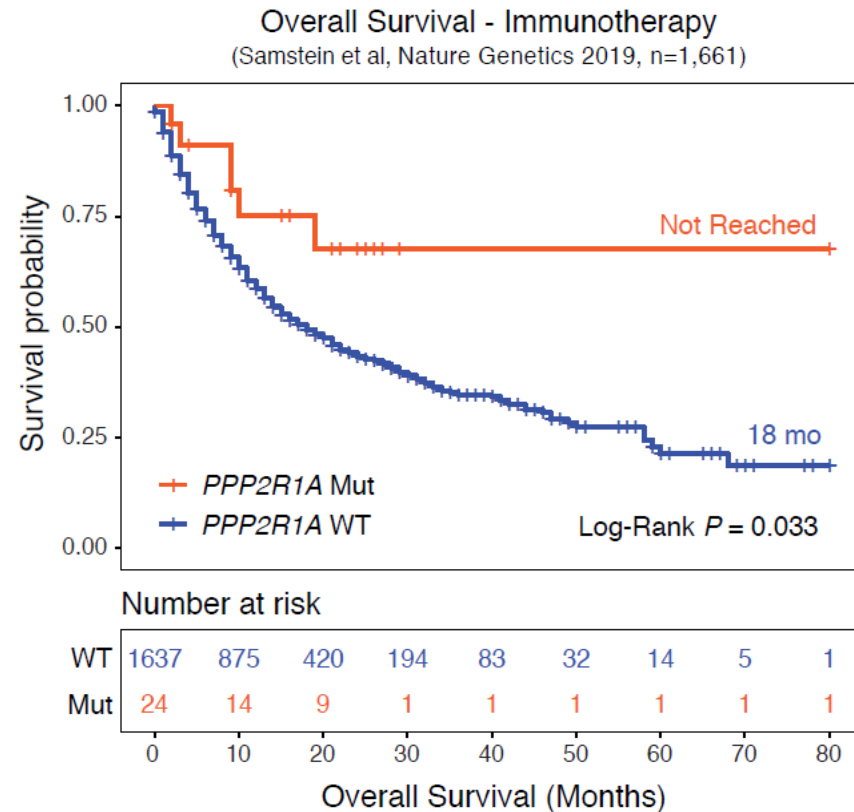
LB-100: Mechanism of action in combination with immunotherapy

LB-100 promotes the production of neoantigens and cytokines and enhances T cell proliferation.

This reinforces the systemic immune response to cancer, thus enhancing the effectiveness of immunotherapy.



PP2A inactivating mutations correlate with increased survival in unselected cancers after immunotherapy



2024 and 2025 milestone publications

nature

Article

PPP2R1A mutations portend improved survival after cancer immunotherapy

<https://doi.org/10.1038/s41586-025-09203-8>

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Check for updates

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Immune checkpoint blockade (ICB) therapy is effective against many cancers, although resistance remains a major issue and new strategies are needed to improve clinical outcomes^{1–5}. Here we studied ICB response in a cohort of patients with ovarian clear cell carcinoma—a cancer type that poses considerable clinical challenges and lacks effective therapies^{6–8}. We observed significantly prolonged overall survival

Molecular
Oncology

COMMENTARY

A single gene mutation predicts response to immune checkpoint blockade in ovarian clear cell carcinoma

Matheus Henrique Dias^{1,2} and René Bernards¹

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Keywords

biomarker; Immune checkpoint blockade; ovarian cancer; Protein Phosphatase 2A

Correspondence

R. Bernards and M. H. Dias, Division of Molecular Carcinogenesis, Oncode Institute,

There is a lack of genetic biomarkers for predicting response to immune checkpoint blockade (ICB) therapy in cancer. The recent discovery that loss-of-function mutations in the gene encoding the protein phosphatase 2A (PP2A) scaffold protein *PPP2R1A* confer sensitivity to immune checkpoint blockade in ovarian clear cell carcinoma, therefore represents a breakthrough. Mechanistically, mutations in the *PPP2R1A* gene induce a strong

RESEARCH ARTICLE

Paradoxical Activation of Oncogenic Signaling as a Cancer Treatment Strategy

Matheus Henrique Dias¹, Anoek Friskes², Siying Wang³, Joao M. Fernandes Neto⁴, Frank van Gemert¹, Soufiane Mourragui⁵, Chrysa Papagianni¹, Hendrik J. Kuiken⁶, Sara Mainardi¹, Daniel Alvarez-Villanueva⁷, Cor Lieftink⁸, Ben Morris⁹, Anna Dekker¹, Emma van Dijk¹, Lieke H.S. Wilms¹, Marcelo S. da Silva^{9,10}, Robin A. Jansen¹, Antonio Mulero-Sánchez¹, Elke Malzer⁶, August Vidal^{1,11,12}, Cristina Santos¹³, Ramón Salazar¹³, Rosangela A.M. Wailemann¹⁴, Thompson E.P. Torres^{14,15}, Giulia De Conti¹, Jonne A. Raaijmakers², Petur Snaebjornsson^{16,17}, Shengxian Yuan¹⁸, Wenxin Qin³, John S. Kovach¹⁹, Hugo A. Armelin¹⁴, Hein te Riele⁴, Alexander van Oudenaarden⁵, Haojie Jin^{1,3}, Roderick L. Beijersbergen^{6,9}, Alberto Villanueva^{7,12}, Rene H. Medema², and Rene Bernards¹

AACR American Association for Cancer Research®

XXXXX 2024 CANCER DISCOVERY | OF2

Report

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The phosphatase inhibitor LB-100 creates neoantigens in colon cancer cells through perturbation of mRNA splicing

Matheus H Dias^{1,6}, Vladislava Liudkovska^{1,2,6}, Jasmine Montenegro Navarro^{1,3}, Lisanne Giebel^{1,3}, Julien Champagne^{1,3}, Chrysa Papagianni^{1,3}, Onno B Bleijerveld^{1,4}, Arno Velds^{1,5}, Reuven Agami^{1,3}, René Bernards^{1,3} & Maciej Cieřła^{1,3}

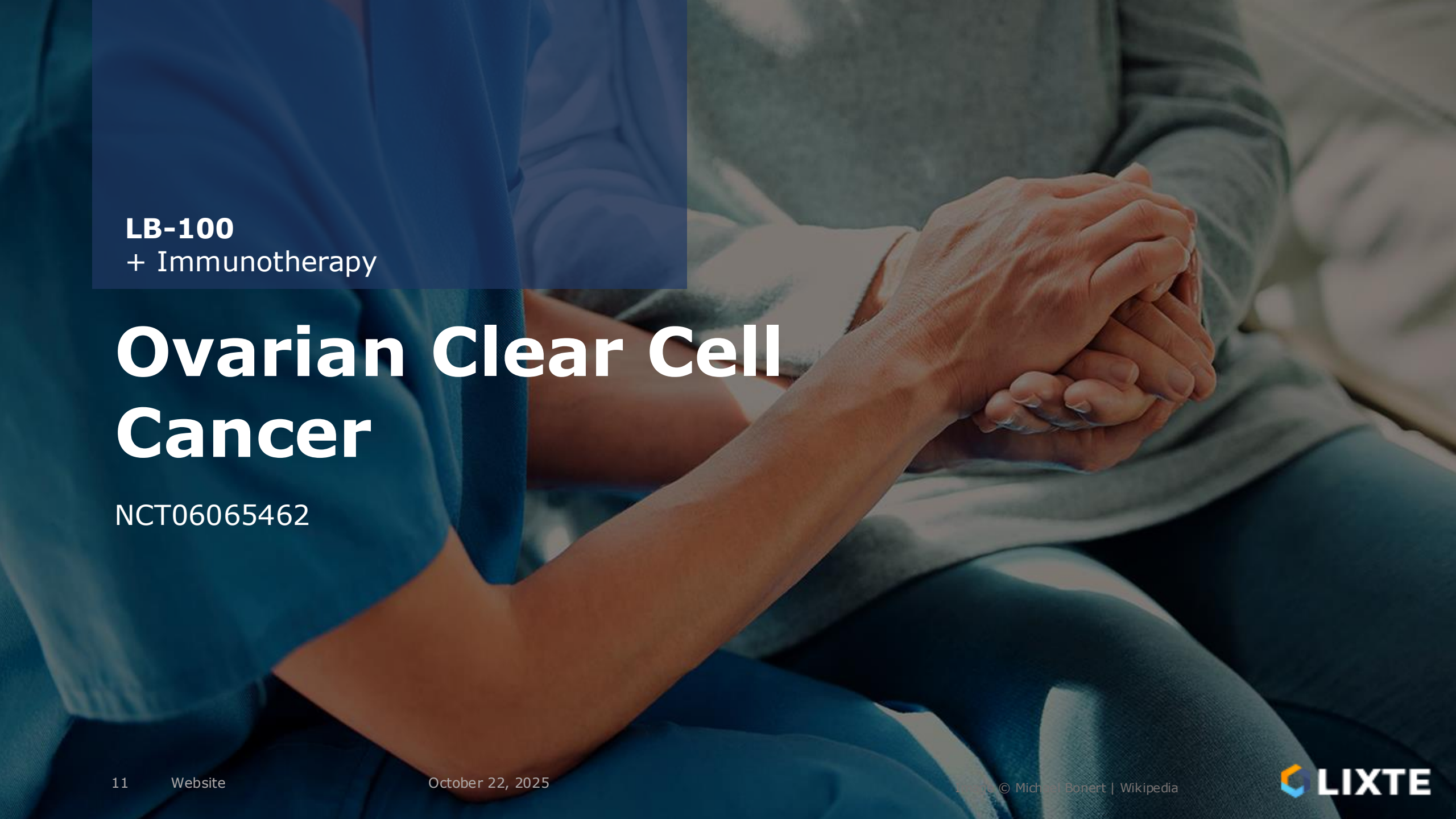
Abstract

Perturbation of protein phosphorylation represents an attractive approach to cancer treatment. Besides kinase inhibitors, protein phosphatase inhibitors have been shown to have anti-cancer activity. A prime example is the small molecule LB-100, an inhibitor of protein phosphatases 2A/5 (PP2A/PP5), enzymes that affect cellular physiology. LB-100 has proven effective in pre-clinical models in combination with immunotherapy, but the molecular underpinnings of

Bottini, 2023). Previous efforts have identified LB-100 as a dual inhibitor of protein phosphatases 2A (PP2A) and 5 (PP5) (D'Arcy et al, 2019). Both phosphatases have a reported function in cancer (Kauko et al, 2020; Vervoort et al, 2021; Zhang et al, 2023), with PP2A considered a tumor suppressor gene given its potential to modulate various cancer-related signaling pathways and thereby inhibiting tumor development (Arroyo and Hahn, 2005; Janssens and Goris, 2001; Junttila et al, 2007). Drug development efforts have therefore focused on small molecule activators of PP2A, as

Building a pipeline in multiple cancer indications

		Pre-Clinical	Phase 1b	Phase 2	Phase 3	Status
LB-100 + Immunotherapy	Ovarian Clear Cell Cancer	NCT06065462				Actively Recruiting at MD Anderson And Northwestern. GSK sponsored, completed enrollment 1b dose escalation.
LB-100 + Immunotherapy	Metastatic MSI Low Colon Cancer	NCT06012734				Open at Netherlands Cancer Institute Roche sponsored.
LB-100 + Chemotherapy	Advanced Soft Tissue Sarcoma (ASTS)	NCT05809830				Completed enrollment 1b dose escalation phase. Full report end 2025

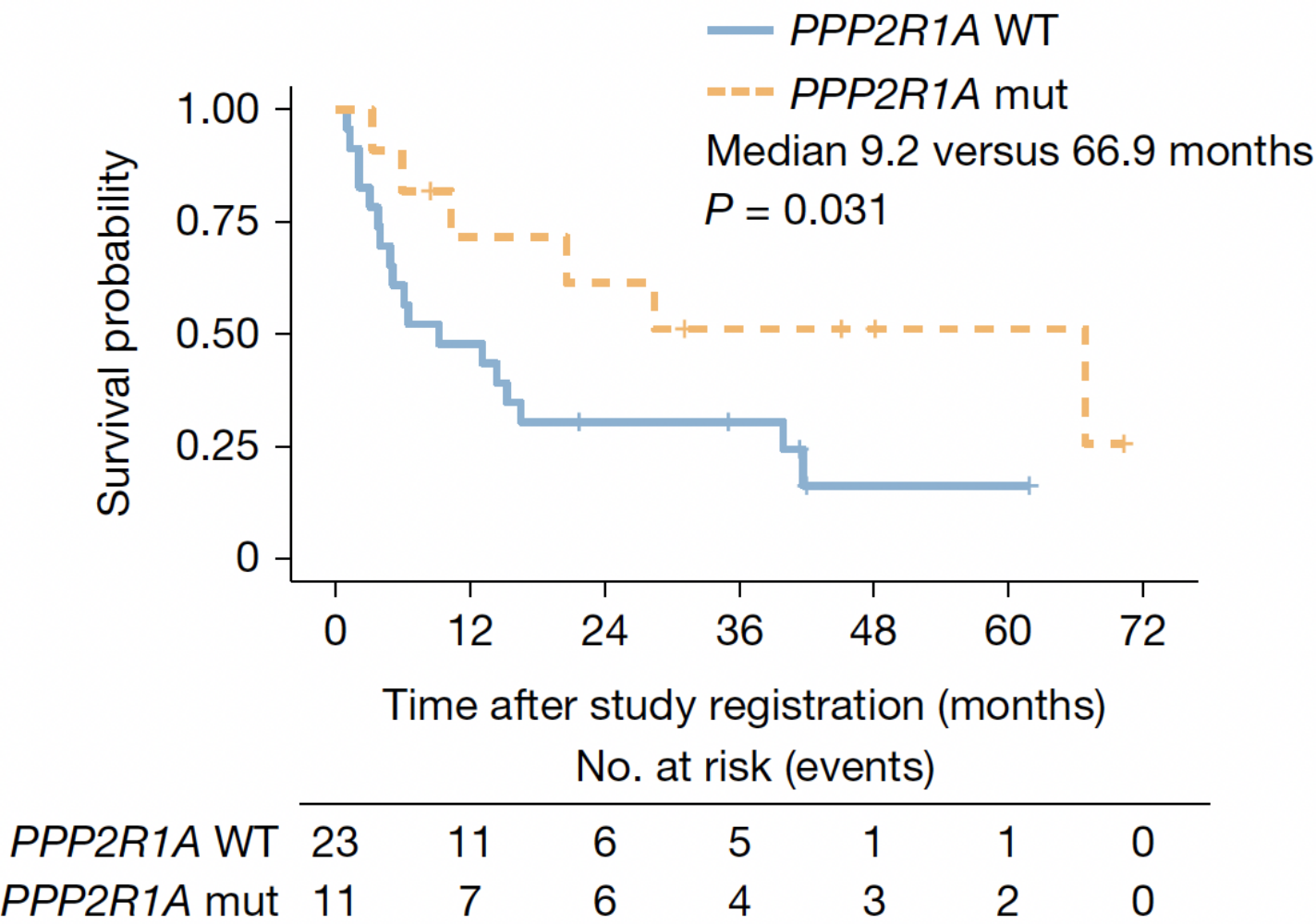


LB-100
+ Immunotherapy

Ovarian Clear Cell Cancer

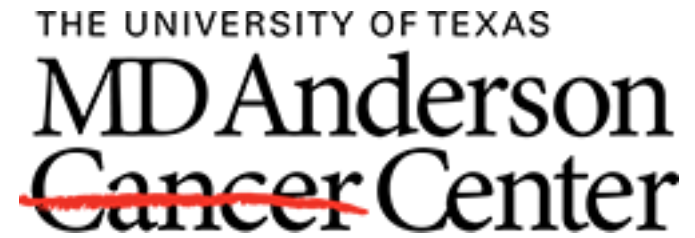
NCT06065462

Loss-of-function mutation in PPP2A shows **67 months** Median Survival in Ovarian Clear Cell Carcinomas Treated with Immune Checkpoint Inhibitors vs **9 months** for wild type



Rationale

- Ovarian Clear Cell Cancer (OCCC) with acquired mutations reducing PP2A activity are more sensitive to immunotherapy
- If LB-100 pharmacologic inhibition of PP2A mimics the effect of mutational reduction in PP2A, LB-100 is expected to enhance immunotherapy in OCCC tumors that do not have mutation



Study design

Ovarian Clear Cell Cancer (OCCC)

A Phase 1b/2 collaborative clinical trial to assess effectiveness of LB-100 combined with GSK's PD-1-blocking monoclonal antibody, dostarlimab,

Funded by GSK and sponsored by the University of Texas MD Anderson Cancer Center, will be conducted at MD Anderson and at Northwestern University's Robert H. Lurie Comprehensive Cancer Center.

Aim is to enroll a total of 21 patients, 6 patients safety intro; patients will be treated up to 24 months or until disease progression.

Status, first 18 patients enrolled, 2nd site open. Complete enrollment second half 2025.

A photograph of an elderly woman with short grey hair, wearing a grey cardigan over a blue and white striped shirt, sitting in a wheelchair. She is smiling and looking towards the right. A younger woman with dark hair, wearing a blue top, is leaning over her from the left, smiling and holding her hands. They are outdoors on a grassy area with trees and hills in the background. A semi-transparent blue rectangle is overlaid on the top left of the image.

LB-100
+ Immunotherapy

Metastatic MSI Low Colon Cancer

NCT06012734

Rationale

- LB-100 stimulates T-Cell Proliferation
- LB-100 influences RNA splicing through unbiased phosphoproteomics
- Generates new antigens for immune stimulation
- Generates an MSI phenotype in MSS tumors
- Validated LB-100 + PD-1 in synergy in multiple pre-clinical models

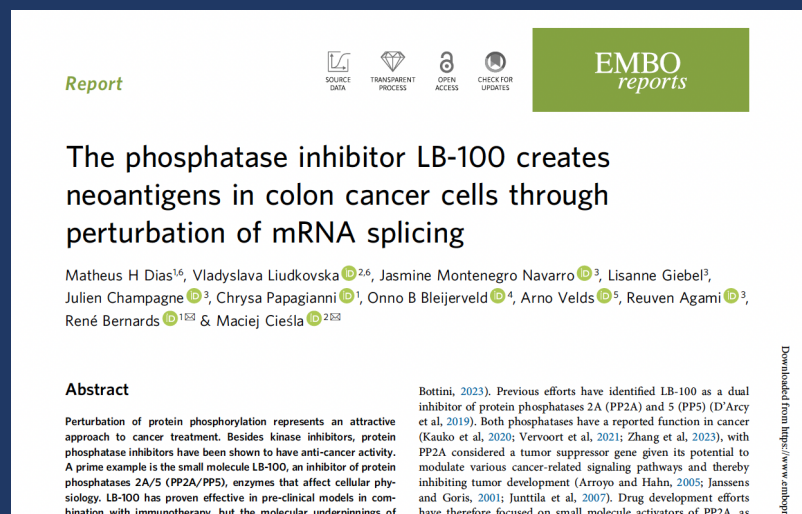


Study design

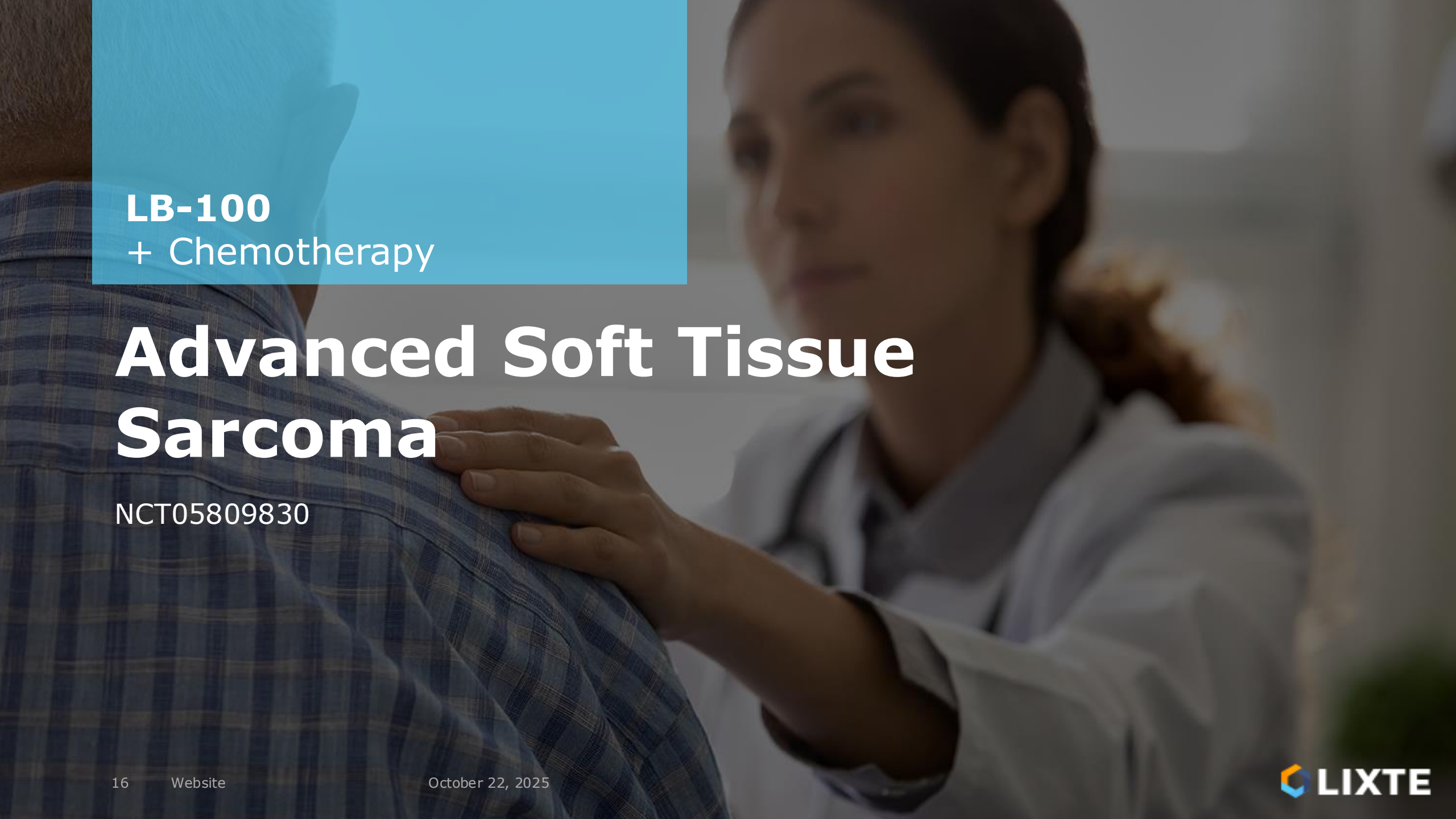
Metastatic MSI Low Colon Cancer
(NCT06012734)

36 patients

First patient enrolled in Q4 2024



Nature Communications volume 12, Article number: 7297 (2021).Protein phosphatase 2A inactivation induces microsatellite instability, neoantigen production and immune response.

A background image showing a doctor in a white coat examining a patient's shoulder. The doctor is a woman with dark hair, and the patient is wearing a blue and white plaid shirt. The image is slightly blurred, focusing on the text overlay.

LB-100
+ Chemotherapy

Advanced Soft Tissue Sarcoma

NCT05809830

Rationale

- ASTS is also a highly aggressive cancer with limited effective treatment
- A single drug, doxorubicin, has been the standard Rx for over 40 years
- In animal models of ASTS, LB-100 markedly improves the effectiveness of doxorubicin

Study design

Phase 1 Trial in
Advanced Soft Tissue Sarcoma (ASTS)
(NCT05809830)

Phase 1: To define the safety of combining LB-100 with doxorubicin.

Multi-center study in collaboration with Grupo Español de Investigación en Sarcomas (GEIS) (PI: Javier Martín Broto MD, Madrid)

Expected completion of first phase Q4 2025



Expanding Horizons in Oncology

Key Preclinical Studies of **LB-100**

Investigators	Tumor Type	Treatment	Outcome
Dias (2024)	Colorectal cancer, pancreatic cancer	+ WEE1 or CHK1	Combination of LB-100 with inhibitors of cellular stress, WEE1 and CHK1 response modulators, was highly effective in killing cancer cells in several pre-clinical cancer models.
Yen (2021)	Colorectal, TNBC, Pancreatic Cancer	+ PD-1	Raises possibility that addition of LB-100 to immunotherapy may be a simple way to convert 'cold' into 'hot' tumors, increasing the percentage of patients responsive to immunotherapy.
Maggio et al (2020)	Glioblastoma	+ PD-1	First preclinical investigation to show that adding LB-100 PP2A inhibition enhances tumor immunotherapy.
Song (2021)	Esophageal squamous cell carcinoma	+ paclitaxel	Data raise the possibility that LB-100 may overcome resistance to paclitaxel.

Led by an experienced and committed team

Our team brings decades of collective expertise in clinical and drug development, ensuring comprehensive knowledge and experience in advancing innovative therapies.



Geordan Pursglove
Chair, CEO and President

An accomplished executive and entrepreneur with 10+ years of experience in M&A, capital markets, strategy, and operations.

Known for innovative leadership across tech, logistics, CX, sports, and marketing, he excels at scaling businesses, raising capital, and executing transformative strategies in public and private markets with a strong, value-driven approach.



Bas van der Baan
CSO

Biotechnology Executive with more than 20 years experience in bringing innovation to the patient. Most recently the Chief Clinical Officer of Agendia

Specialized in precision oncology and business development. Extensive experience in clinical development overseeing numerous clinical trials from start to publication.



Peter Stazzone
CFO

Seasoned CFO with 25 years of expertise in finance operations management and accounting across start-ups, high-growth ventures, and multi-billion-dollar enterprises. Since 2018, he has served on the Board of Directors of Beyond Commerce and as Chairman of the Audit Committee, Peter holds an MBA in Finance from DePaul University and a BS in Accounting from the University of Illinois at Urbana-Champaign and is a Certified Public Accountant (CPA).

Supported by world-class experts & partners

Collaborating with esteemed key opinion leaders and top-tier organizations amplifies our strengths

Scientific Advisory Committee



Prof. René Bernards

- Leader in the field of molecular carcinogenesis
- Extensive experience in cancer drug development
- International member, National Academy of Sciences, US



Yun Yen MD, PhD, FACP

- Distinguished cancer investigator
- Former Chairman Mol. Pharmacology City of Hope
- Former President of Taipei Medical University



Stephen Forman, MD

- International KOL in hematological cancers
- Professor of Hematology & Hematopoietic Cell Transplantation City of Hope National Medical Center

About LIXTE



Clinical-stage pharmaceutical company developing a new class of cancer therapy called PP2A inhibitors.

Unique



Our innovative approach enhances the efficacy of chemotherapies and immunotherapies, potentially providing new options for cancer patients.

Big Impact



Our proprietary compound LB-100 acts as a safe and potent inhibitor of PP2A.

Strong Mechanism
Of Action



Conducting multiple clinical trials for solid tumors, including Advanced Soft Tissue Sarcoma Ovarian Clear Cell Cancer and Small Cell Lung Cancer.

Clinical Stage



JOIN US

**in our mission to bring
the first PP2A inhibitor
to cancer patients.**

Get in Touch

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