Lin BioScience

Blindness & Cancer

2022

Novel Treatment for Unmet Medical Need

Lin Bioscience is a clinical stage drug development company focused on sourcing/advancing novel therapeutic candidates in areas with significant unmet need. The Company's pipeline consists of RBP4 IP portfolio, CDC7 platform technology and 4 distinct small molecule drug candidates. LBS-008, targeted to treat Stargardt disease and dry age-related macular degeneration ("Dry AMD"), and LBS-009, targeted to treat NASH, derived from the RBP4 IP portfolio, are developed by Belite Bio, a subsidiary company of Lin BioScience. LBS-007, developed from the CDC7 platform technology and targeted to treat various cancers, and LBS-002, targeted to treat glioblastomas and metastatic brain tumors, are developed by Lin BioScience.

LBS-007 is a non-ATP competitive CDC7 inhibitor for the treatment of a broad array of cancers, especially for refractory/relapsed and late-stage cancers such as AML, ALL, ovarian cancer, pancreatic cancer, etc., which is expected to enter phase 1 in 2022.

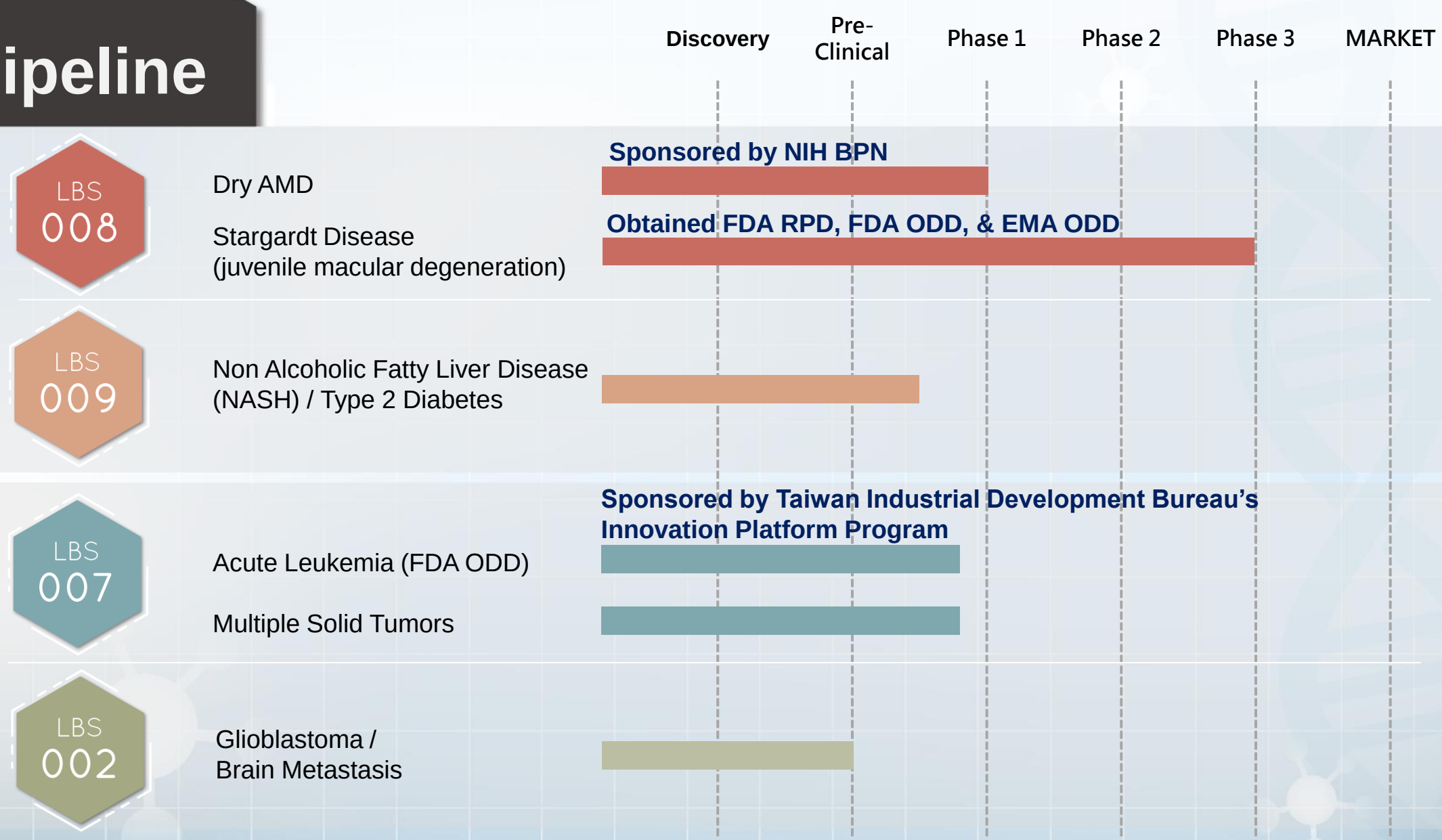
LBS-008 is the only drug candidate intended to treat dry AMD within the current drug development projects of the NIH Blueprint Program ("BPN"), whose mission is to foster small-molecule neurotherapeutic development. The mechanism of action utilized by LBS-008 has been recognized and recommended as a priority for clinical development in both STGD1 and dry AMD in a systematic review published by the U.K. National Institute for Health Research, or the NIHR, in 2018. LBS-008 has initiated its phase 3 for Stargardt disease and expects to initiate its phase 3 for dry age-related macular degeneration in 2022.

COLUMBIA UNIVERSITY

NIH National Institutes of Health

NIH Blueprint Neurotherapeutics Network

Pipeline


Discovery
Pre-Clinical
Phase 1
Phase 2
Phase 3
MARKET
Developed by Belite Bio™
RBP4 IP Portfolio
LBS 008
Dry AMD
Stargardt Disease (juvenile macular degeneration)
Sponsored by NIH BPN
Obtained FDA RPD, FDA ODD, & EMA ODD
LBS 009
Non Alcoholic Fatty Liver Disease (NASH) / Type 2 Diabetes
Developed by Lin BioScience
Oncology Programs
LBS 007
Acute Leukemia (FDA ODD)
Multiple Solid Tumors
Sponsored by Taiwan Industrial Development Bureau's Innovation Platform Program
LBS 002
Glioblastoma / Brain Metastasis

Management Team

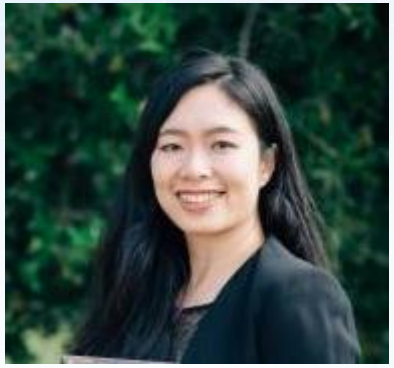
Tom Lin, MMED, PhD, MBA (CEO)

- **10 years of executive management role in biotech, incl. 2 IPO**
- **Multidisciplinary Specialization Clinical Training & Research in Neuroscience, Cardiovascular & Renal Medicine, Oncology, Immunology & Immunotherapy**
- **Over 10 new drug developments in multiple therapeutic areas, including Ophthalmology, CNS, Cardiovascular, Oncology, Immuno-Oncology, Immunotherapies, Immunosuppressants**
- **Drug development experience from drug discovery to Phase 3**

- **PhD in Medicine - University of Sydney**; Specialization: Neurology & Immunology
  - Treatment Strategies for Autoimmune Neuropathies
- **Specialist Certificate in Clinical Neuroscience - University of Melbourne**; Specialization: Neurology
  - Neurological Disorders, Neuroimaging & Diagnostics
  - Clinical Research & Design
- **Master of Medicine - University of Sydney**; Specialization: Multidisciplinary Medicine and Surgery
  - Medicine: Cardiovascular & Renal Medicine, Neonatal Medicine
  - Surgery: Vascular & Endovascular Surgery, Transplant Surgery
- **Cancer Therapeutics & Research Certificate - Harvard Medical School**
- **Master of Business Administration - Columbia University, London Business School, HK University**
- **Extensive Drug development from preclinical to global phase 3 trials**
  - Phase 1 – RBP4 Inhibitor for the Treatment of Atrophic Macular Degeneration & Stargardt Disease
  - Phase 2 – Oubain Antagonist in the Treatment of Essential Hypertension
  - Phase 2 – SERCA2a Inhibitor in the Treatment of Acute Heart Failure
  - Phase 2 – Pan-HER Inhibitor in the Treatment of HER2+ Breast Cancer and Gastric Cancer
  - Phase 3 – Anti-Glycan Active Immunotherapy in the Treatment of Metastatic Breast Cancer
  - Phase 3 – Anti-α4 integrin Antibody in the Treatment of Resistant-Refractory Multiple Sclerosis
  - Phase 2 – mTOR Immunosuppressant in the Treatment of Autoimmune Peripheral Neuropathies
  - Co-invented and applied 64 patents

Management Team

Irene Wang, PhD, MBA (CSO)



- PhD in Biochemical Sciences, National Taiwan University, Trained at Scripps Research (TSRI), MBA from UCSD
- Co-invented and applied 125 patents and published 6 papers
- Extensive Drug development from preclinical to global phase 3 trials

Hao-Yuan Chuang, CFA, MBA, FRM (CFO)

- MBA from Columbia University
- Served as Executive/Director positions, led transactions: Suning – US$320M acquisition of Inter-Milan; Wanda – US$10B property acquisition, bond issue and IPO; CITIC Securities International – Finance Advisor to Agricultural Bank of China's US$22B IPO

Yvonne Chen (COO)

- Certified pharmacist & master in Science (Medicinal Chemistry) from National Taiwan University
- Vast experience in clinical trial management and regulatory submissions with over 50 studies in various indications
- Served as Global Project Lead and Manager in Pfizer Taiwan

Ophthalmology Clinical Advisory Board

Global leading experts on dry age-related macular degeneration and Stargardt disease

- **Dr. Frank Holz:** Chairman of Ophthalmology, University of Bonn

- **Dr. Michel Michaelides:** Consultant Ophthalmologist at Moorfields Eye Hospital and Professor of Ophthalmology, UCL Institute of Ophthalmology

- **Dr. Quan Nguyen:** Professor of Ophthalmology, Stanford University

- **Dr. Hendrik P.N. Scholl:** Co-Director of the Institute of Molecular and Clinical Ophthalmology, Basel & Professor and Chairman of the Department of Ophthalmology, University of Basel, and Adjunct Professor of Ophthalmology at the Wilmer Eye Institute, Johns Hopkins University

- **Dr. Robyn Guymer:** Professor of Ophthalmology, University of Melbourne & Deputy Director of the Centre for Eye Research Australia

LBS-008
FOR DRY AMD & STARGARDT DISEASE

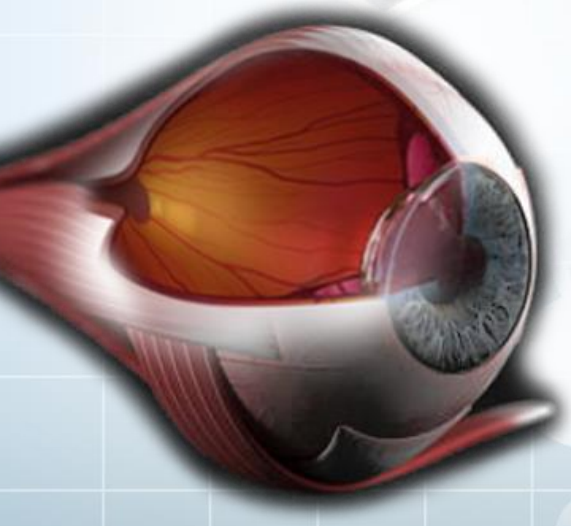
LBS 008

BRING

HOPE TO INCURABLE BLINDESS

For dry AMD & Stargardt Disease

- Discovery
- Preclinical
- Phase 1
- Phase 2
- Phase 3
- MARKET



KEY OPPORTUNITY

Zero Approved Treatments

FDA RPD ODD

for Stargardt (US & EU)

NIH **Blueprint**

“a promising first-in-class oral medication intended to slow or halt the progression of dry AMD”

Dry AMD MARKET

11M

AMD patients in the US (90% are dry AMD)

$255B

estimated global direct healthcare cost of dry AMD

STGD1 MARKET

1 in 10,000

Stargardt Disease Juvenile onset macular degeneration

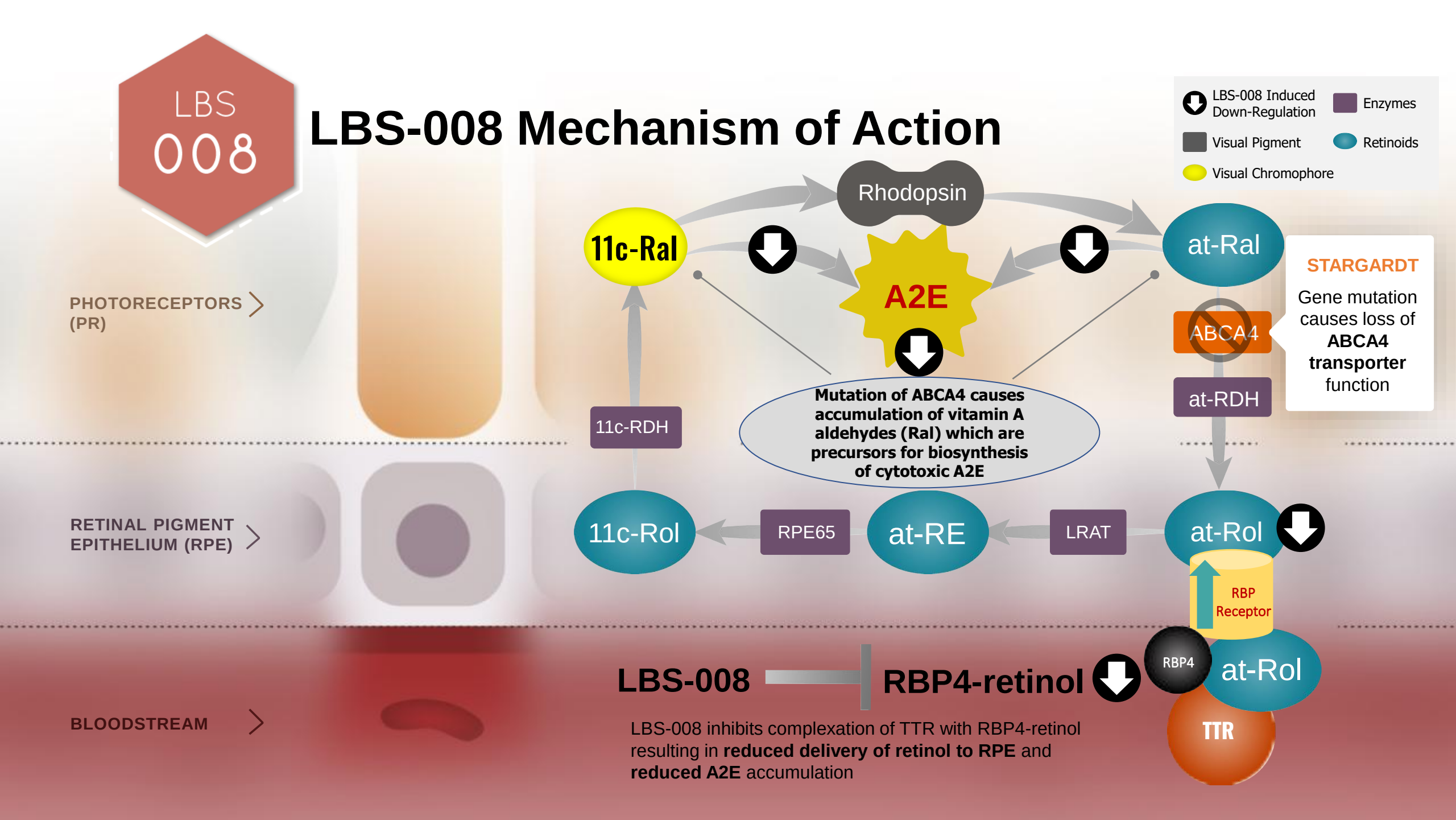
30,000

STGD1 patients in the US

Reference: Globaldata, Lancet, Orphanet, STEM CELLS Translational Medicine

LBS 008

LBS-008 Mechanism of Action



LBS-008 ⊣ **RBP4-retinol**

LBS-008 inhibits complexation of TTR with RBP4-retinol resulting in **reduced delivery of retinol to RPE** and **reduced A2E** accumulation

LBS 008

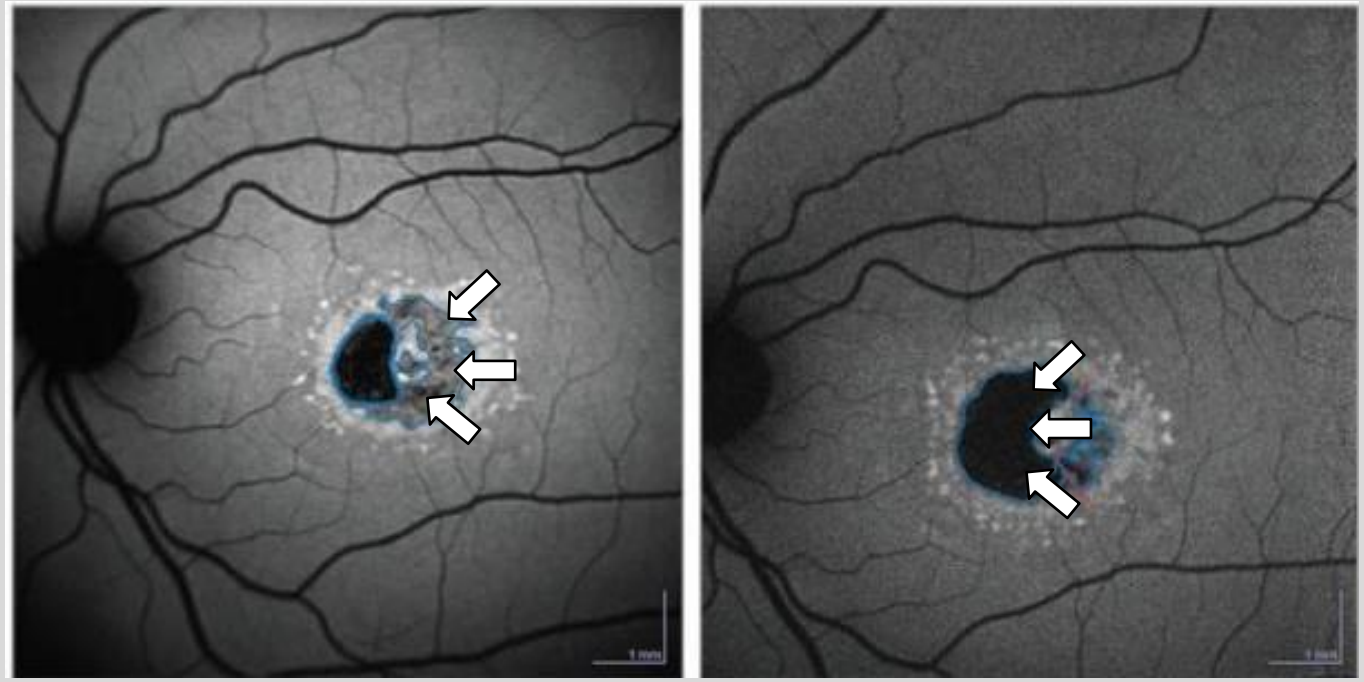
Pathogenesis of STGD1

Case Study in the ProgStar study:

- Fundus autofluorescence (FAF) photography from a STGD1 patient at ‘baseline’ and 22 months later showed that the autofluorescence (i.e, bisretinoid-laden lipofuscin) precedes lesion growth. The pattern (type of FAF) and nature of the lesions (unifocal versus multifocal lesions) can predict lesion growth location and rate.

Central Lesion in STGD1 patient at ‘baseline’

Same Lesion in STGD1 patient 22 mos later



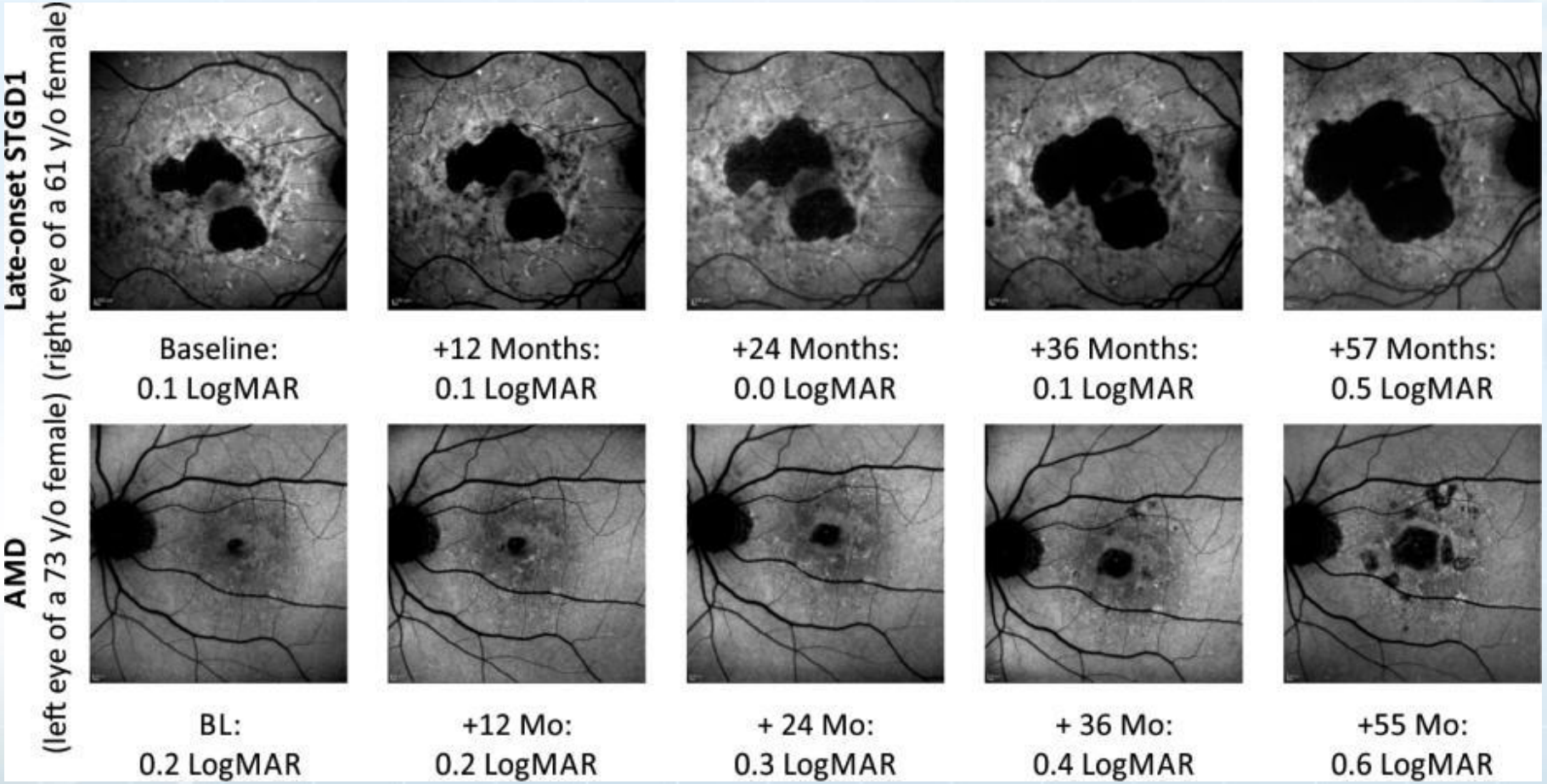
- The arrows point to areas of questionably decreased autofluorescence (QDAF) into which the central lesion advances.

Reference: The ProgStar Study Group, **Ophthalmology**, 2016; 123

LBS 008

STGD1 and dry AMD share a similar pathophysiology which is characterized by the aberrant and excessive accumulation of cytotoxic bisretinoid fluorophores, subsequent retinal atrophy, and vision loss

Pathogenesis of STGD1 & Dry AMD



Reference: Lindner et al. Differential Disease Progression in Atrophic Age-Related Macular Degeneration and Late-Onset Stargardt Disease. Invest Ophthalmol Vis Sci. 2017;58(2):1001-1007.

LBS 008

Symptoms of STGD1 & Dry AMD

Symptoms of STGD1

Normal
Central Vision

Blurry & Distorted
Central Vision

Lost
Central Vision

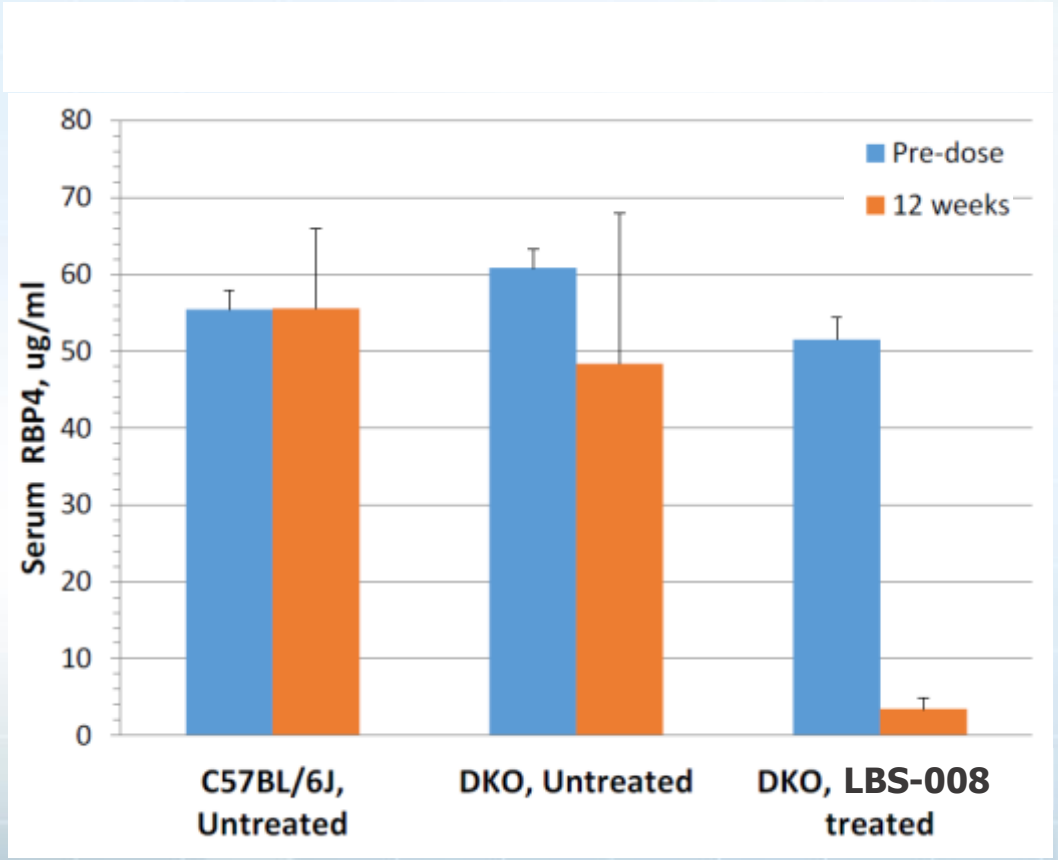
Symptoms of Dry AMD

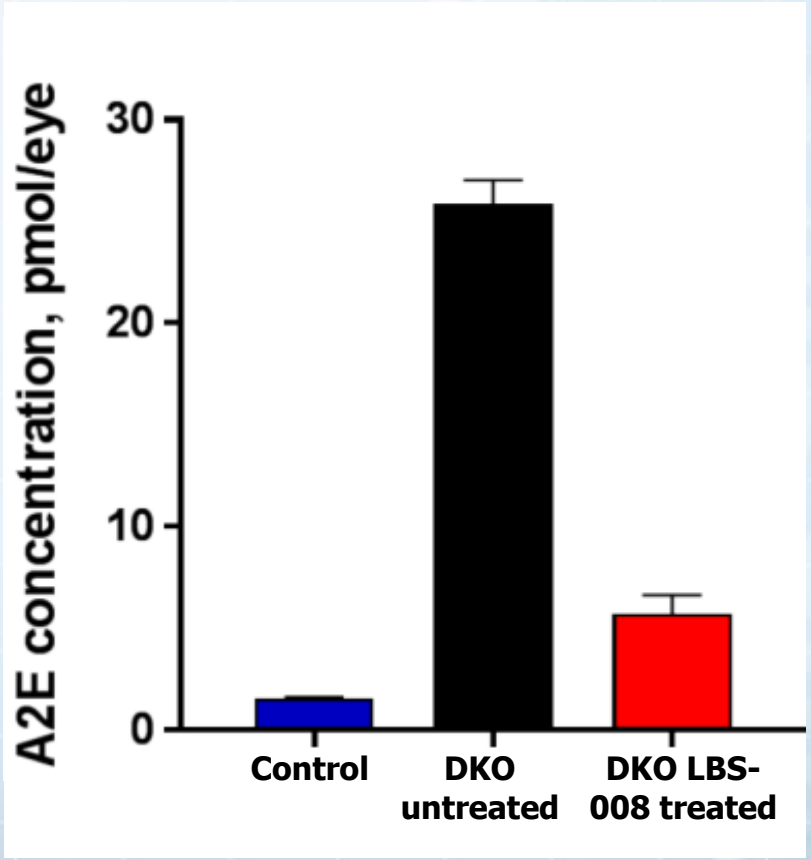
Reference:
https://makariwellness.com/stargardt-disease/
https://www.ncbi.ie/supporting-you/everyday-living/eye-conditions/age-related-macular-degeneration-amd/

Effect of LBS-008 on biomarkers in a STGD1 mouse model (ABCA4-/-/RDH8-/-)

RBP4 Reduction Reduces A2E Accumulation by 80%

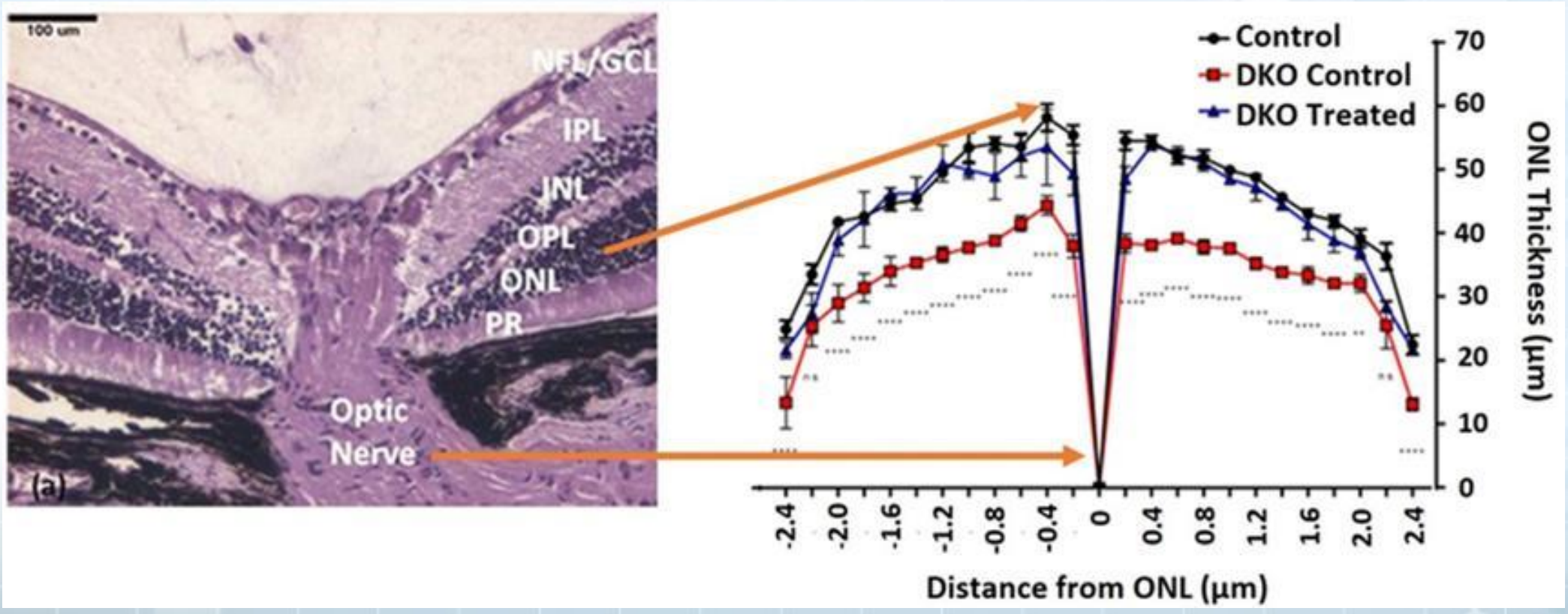
- Daily dosing at approx. 25mg/kg of LBS-008 for 12 weeks (LBS-008-supplemented chow *ad libitum*).
- A mean RBP4 reduction of ~90% in LBS-008 treated mice led to an ~80% reduction in A2E compared to untreated ABCA4$^{-/-}$/RDH8$^{-/-}$ double knockout (DKO) mice.





RBP4 Reduction Preserves Photoreceptor Cells

- **Outer Nuclear Layer (ONL)** thickness was significantly decreased in untreated ABCA4$^{-/-}$/RDH8$^{-/-}$ mice, compared to mice treated with LBS-008
- **Macular degeneration in Dry AMD and STGD1** is associated with **thinning of the ONL which indicates loss of photoreceptor cells**



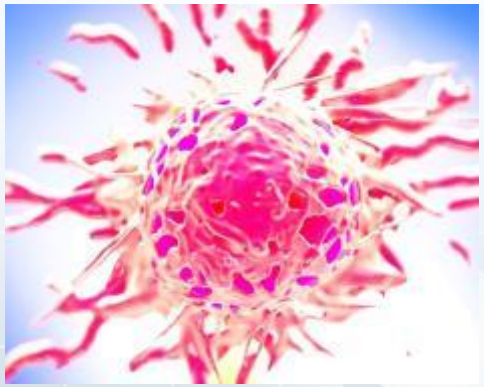
LBS-007
FOR BROAD VARIETY OF CANCERS

LBS 007

- DISCOVERY
- PRE-CLINICAL
- PHASE I
- PHASE II/III
- MARKET

Natural non-ATP CDC7 Inhibitor

for treatment of Broad Variety of Cancer types



KEY OPPORTUNITY

Novel Anti-Cancer
Target Therapy

FDA ODD
for ALL (US)

MARKET

$5B
Expected 2026 market size of AML & ALL

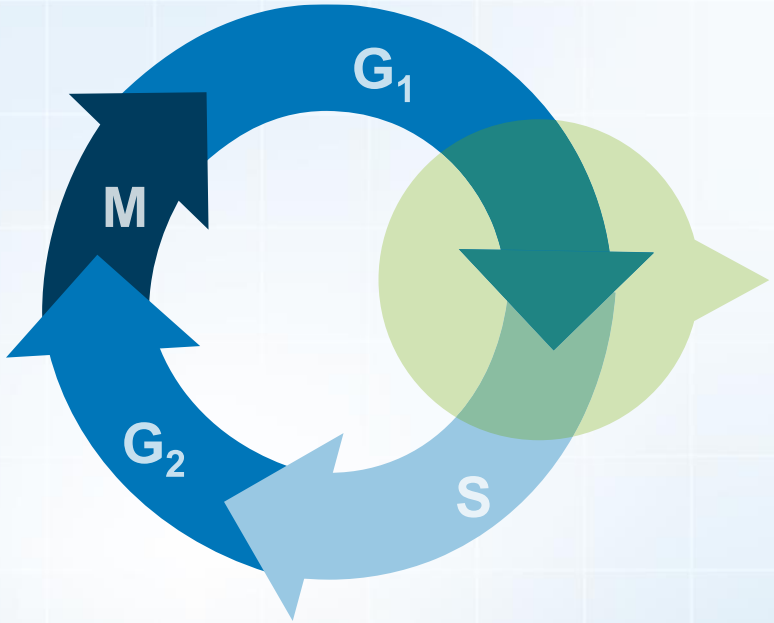
1.7 in 100k
Acute lymphoblastic leukemia (orphan disease)

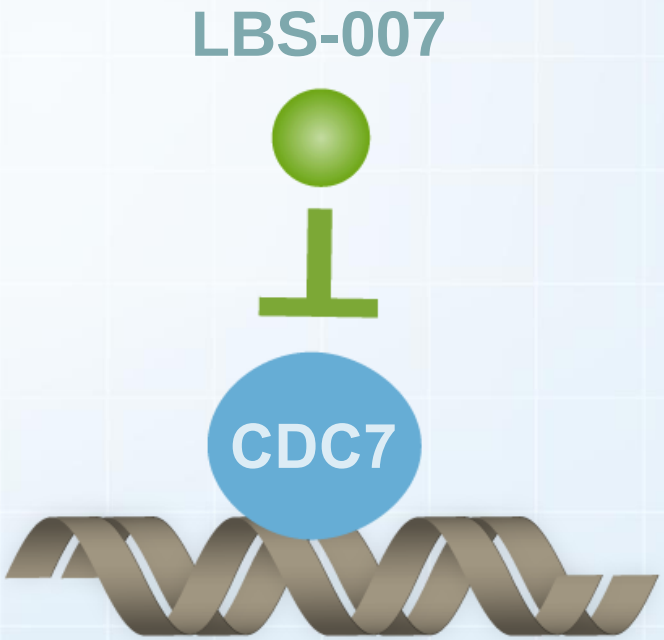
$55B
Expected 2023 market size of pancreatic, lung, ovarian cancers

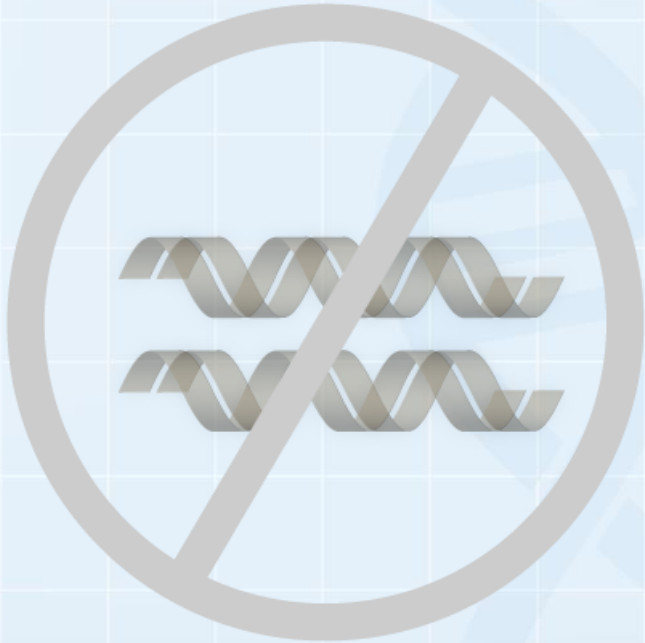
$6B
Estimated global market

Reference: Globaldata, Marketwatch, NIH National Cancer Institute

Inhibits CDC7 in Cell Cycle Regulation







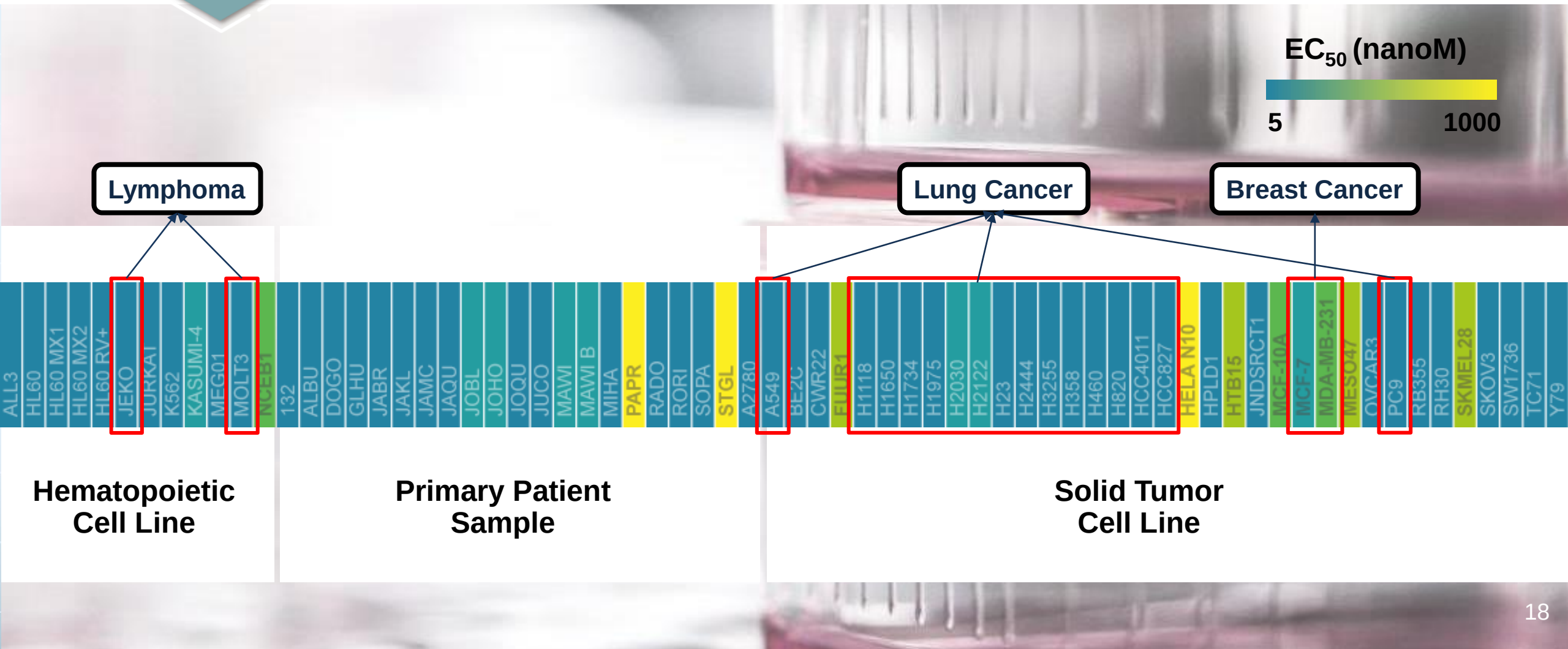
1 TARGETS
S Phase Progression

2 INHIBITS
CDC7's role in
DNA Replication

3 PREVENTS
Cell Division

LBS 007

Potently Inhibits Multiple Cancer Cell Lines & Primary Patient Samples of Blood Cancers

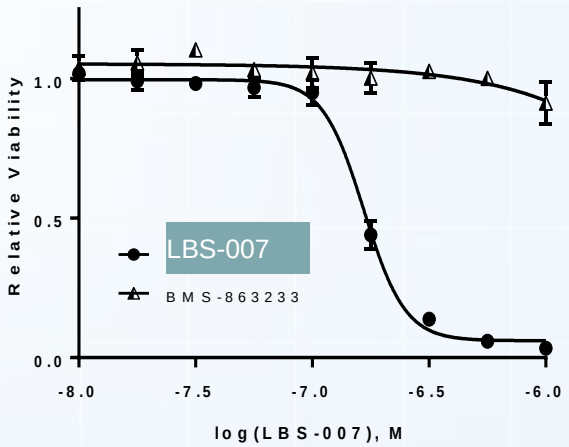


LBS-007 works well on small cell lung cancer and pancreatic cell lines

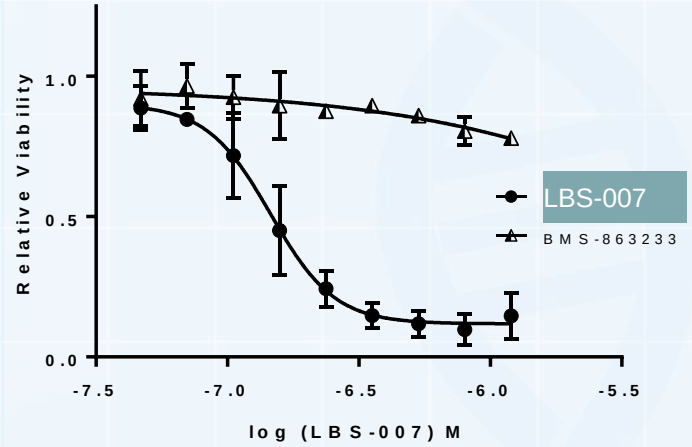
- LBS-007 achieved sub-μM (~150 nM) concentration efficacy against cancer cell lines
  - Small Cell Lung Cancer
  - Pancreatic Cancer

- LBS-007 performed better than
  - Cisplatin, a solid tumor drug with strong toxicity side effects
  - BMS-863233, an excellent CDC7 inhibitor from Bristol-Myers Squibb

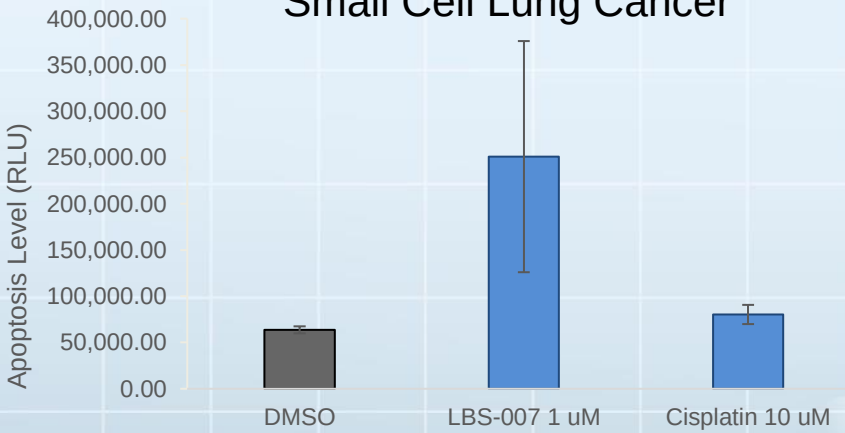
Pancreatic Cancer



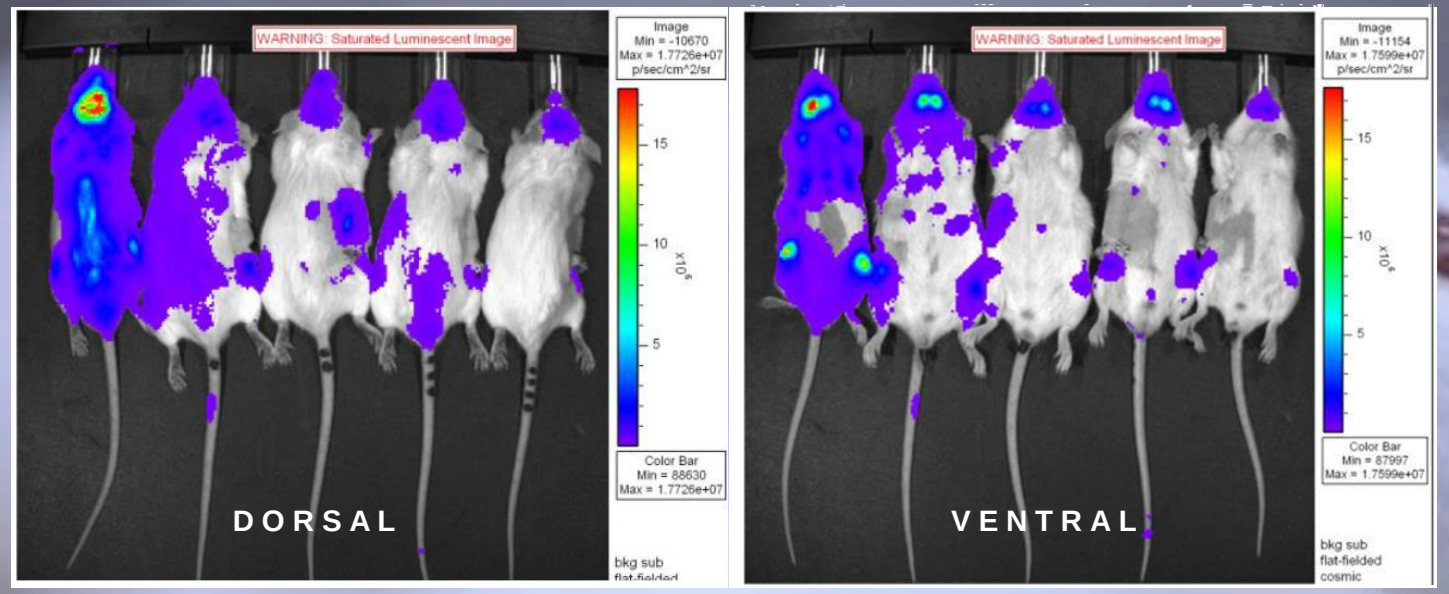
Small Cell Lung Cancer



Small Cell Lung Cancer



LBS-007 – Effective Against Blood Cancers



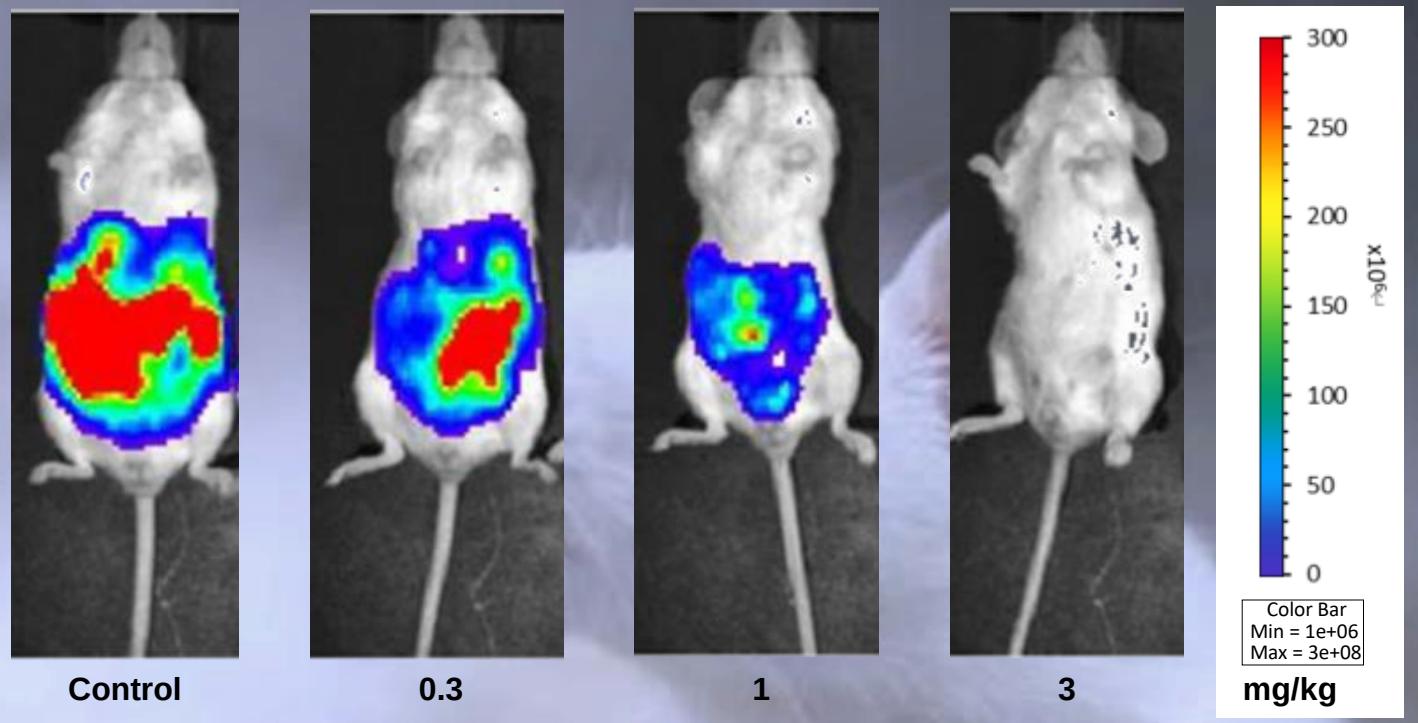
DOSE-RESPONSIVE MANNER

Inhibits **TKI-Resistant Acute Lymphoblastic Leukemia (ALL)** growth *in vivo* using a continuous infusion regimen

Reference: Unpublished data from Dr. Mark Frattini

LBS-007 – Also Effective Against Solid Tumors in Animal Models

Inhibits **Ovarian Tumor** growth *in vivo*



Reference: Unpublished data from Dr. Mark Frattini

Thank You

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Lin BioScience

Blindness & Cancer

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