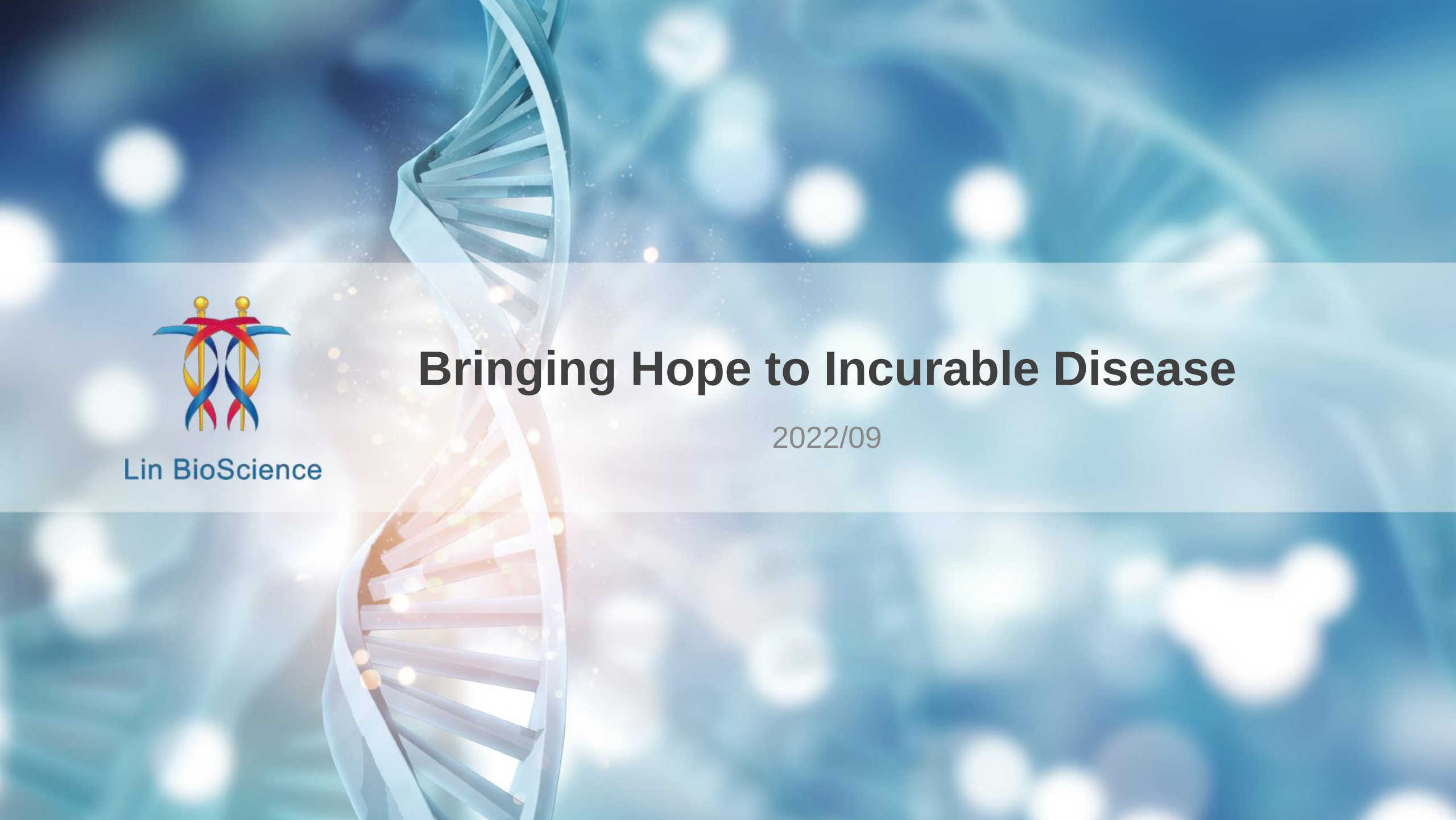

Lin BioScience

Bringing Hope to Incurable Disease

2022/09

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Novel Treatment for Unmet Medical Need

Lin BioScience, Inc. (TW TPEx: 6696) is a drug development company established in 2016 focusing on advancing novel therapies and first-in-class treatments for unmet medical needs in various therapeutic areas such as ophthalmology, oncology, and metabolic diseases. The Company's pipeline consists of RBP4 IP portfolio, CDC7 IP portfolio 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-007 treating ALL has been granted orphan drug designation (ODD) in the U.S..

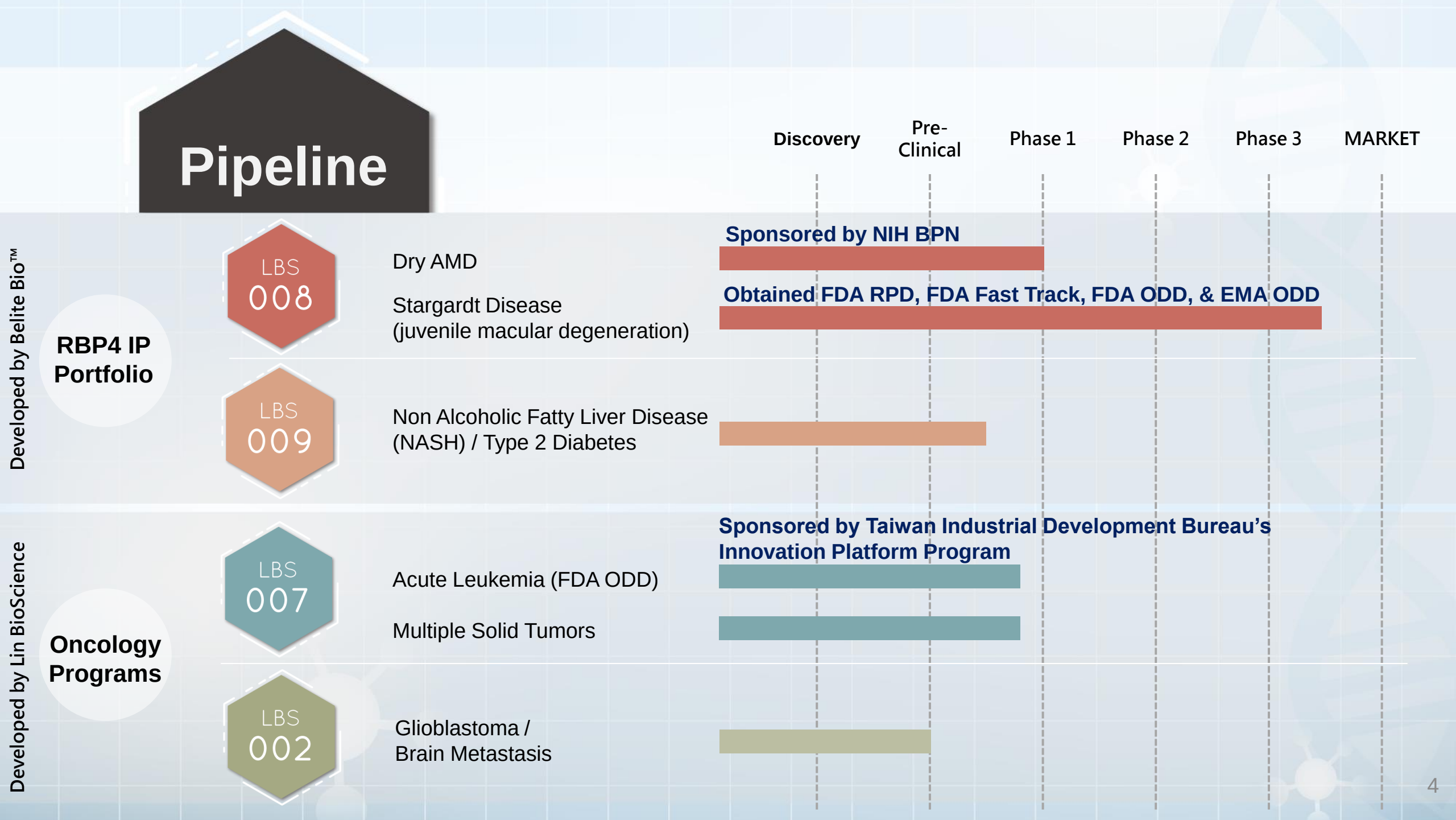
LBS-008 is the only drug candidate intended to treat dry AMD within the current drug development projects of the NIH Blueprint Program ("BPN"), whose mission is to foster small-molecule neurotherapeutic development. The mechanism of action utilized by LBS-008 has been recognized and recommended as a 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. LBS-008 has been granted fast track designation, rare pediatric disease designation (RPD) in the U.S., and orphan drug designation (ODD) in the U.S. and Europe.

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 Fast Track, 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

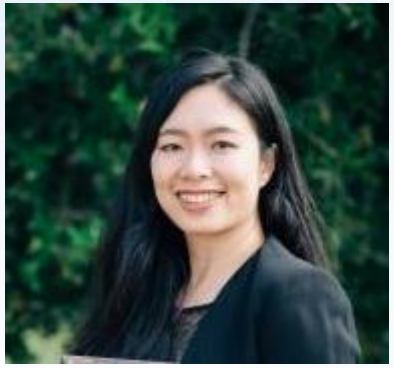
Tom Lin, MMED, PhD, MBA
(Chairman)

- **10+ years of executive management role in biotech, incl. 4 IPO (Lin BioScience & Belite)**
- **Multidisciplinary Specialization Clinical Training & Research in Neuroscience, Cardiovascular & Renal Medicine, Oncology, Immunology & Immunotherapy**

- **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 (President & CSO)



- PhD in Biochemical Sciences, National Taiwan University, Trained at Scripps Research (TSRI), EMBA from University of California San Diego
- Co-invented and applied 125 patents and published 6 papers
- Extensive Drug development from preclinical to global phase 3 trials and **3 IPOs (including Lin BioScience and Belite Bio)**

Yvonne Chen (COO)

- Certified pharmacist & master in Science (Medicinal Chemistry) from National Taiwan University
- Served as Global Project Lead and Manager in Pfizer Taiwan
- Vast experience in clinical trial management and regulatory submissions with over 50 studies in various indications and **3 IPOs (including Lin BioScience and Belite Bio)**

陳菀姍, CPA (Finance Director)

- Certified Public Accountant & master in accounting from National Taipei University.
- Finance manager in a Taiwan biotech company and as assistant manager of audit department in Deloitte Taiwan
- Vast experience in auditing of listed companies and **initial public offering (including Lin BioScience and Belite Bio)**

LBS-008
FOR DRY AMD & STARGARDT DISEASE

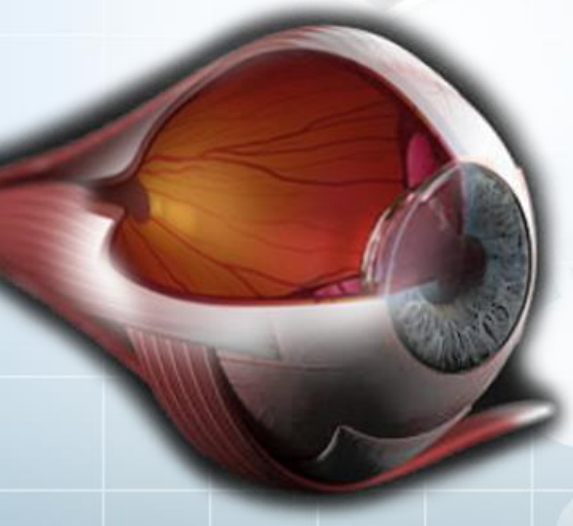
LBS 008

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 FT
for Stargardt (US & EU)

COLUMBIA UNIVERSITY

NIH **Blueprint**

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

資料來源:
https://www.ninds.nih.gov/About-NINDS/Impact/Translational-Research-Success-Stories

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

資料來源:
Globaldata, Lancet, Orphanet, STEM CELLS Translational Medicine

PRODUCT HIGHLIGHTS

Oral treatment for an unmet market

- **Belite Bio's lead asset LBS-008** is a novel**, orally administered, Retinol Binding Protein 4 ("RBP4") antagonist** intended to slow or halt progression of vision loss in Stargardt disease (STGD1) and dry AMD.
- Currently **no approved treatments** for either STGD1 or dry AMD, significant market opportunity to become **Standard of Care**.
- Clinical development approach **endorsed by US NIH**, specifically **to treat dry AMD**.
- **UK NIHR's** 2018 systematic review of >7,000 publications recommends RBP4 antagonists as a **priority for clinical development to treat both STGD1 and dry AMD**.
- Dry AMD afflict **11 million patients** in the US and **196 million patients** worldwide.
- Without treatment, the continual increase in the size of the elderly population will worsen the impact of this disease.
- STGD1 is an orphan disease affecting approx. 1 in 10,000 children and adults.
- Granted **Fast Track Designation, Rare Pediatric Disease** in US / **Orphan Drug Disease** designation in US and EU for STGD1.
- **Priority Review Voucher (PRV)** eligible, vouchers have sold for $80M-$125M.

CLEAR CLINICAL DEVELOPMENT PATHWAY

Reduction in Lesion Growth Rate as Measured by Retinal Imaging is an FDA Accepted Primary Endpoint in STGD1 and dry AMD

Completed

Phase 1

- Completed, double-blind
- US SAD + AU SAD/MAD: 111 healthy adults
- **Well tolerated and reduced mean RBP4 by ≥70% from baseline**

Ongoing

Phase 1b/2 Adolescent STGD

- Open-label, Phase 1b completed, Phase 2 ongoing
- AU/TW Ph1b: 11 subjects completed
- AU/TW Ph2 (2-yr): 13 subjects
- **Achieved a mean RBP4 reduction of > 70% without severe adverse events**

Phase 3 Adolescent STGD

- Initiated, double-blind
- Global study (2-yr): 60 subjects
- Primary end point: change in lesion growth rate by retinal imaging

Planned

Phase 2/3 Dry AMD

- Expect to start in 2022, randomized, double-blind
- Intermediate to advanced stage dry AMD
- Global study
- To evaluate the safety and efficacy

STGD NDA PRV

- PRV sale (in the last 3 years, price range $80-125 million)

Dry AMD NDA

- In-licensed **9 active patent families**
- Composition of matter patents expected to expire **2034-2035** without patent term extension

CLINICAL TRIAL DESIGN FOR STGD1

	STDG1 phase 2	STGD1 phase 3 ("DRAGON")
Enrollment	13 participants	60 participants
Sites	Aus & TW	Global
Masking	Open Label	Double Blind
Placebo	N/A	2:1 ratio (LBS-008 : Placebo)
Duration	2 years	2 years
Primary measures	Safety & Tolerability, optimal dose	Safety & Tolerability, Efficacy (Lesion size growth, DDAF)
Other measures	Lesion size (DDAF), QDAF, BCVA, SD-OCT, microperimetry	QDAF, BCVA, SD-OCT, microperimetry

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/

Lin BioScience

LBS-008 Clinical Data

LBS 008

INTERIM PHASE 2 RESULTS

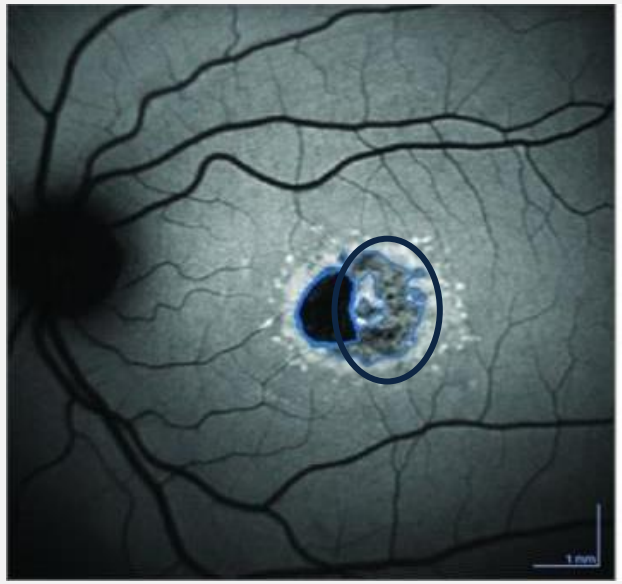
Summary of Related Adverse Events

Adverse Events	Severity	Relationship to Drug	Frequency (#patients)	% Recovered	% On-going
Xanthopsia	Mild	Definitely Related	6/13	3/6 (50%)	3/6 (50%)
Delayed Dark Adaptation	Mild	Definitely Related	8/13	1/8 (12.5%)	7/8 (87.5%)
Night Vision Impairment	Mild	Definitely Related	1/13	0/1	1/1 (100%)
Increasing error score on FM100	Mild	Probably Related	1/13	0/1	1/1 (100%)

- All instances of DDA and Xanthopsia were **mild** and **transient**
- Subjects shown to have DDA based on laboratory measure were mostly **asymptomatic**
- One subject recorded to have an increasing error score on FM100 test (tests color vision and color perception) showed only a **mild** impact
- **No severe AEs or SAEs** reported and no AEs requiring discontinuation of treatment
- **No clinically significant** findings in relation to vital signs, physical exams or electrocardiograms

LBS 008

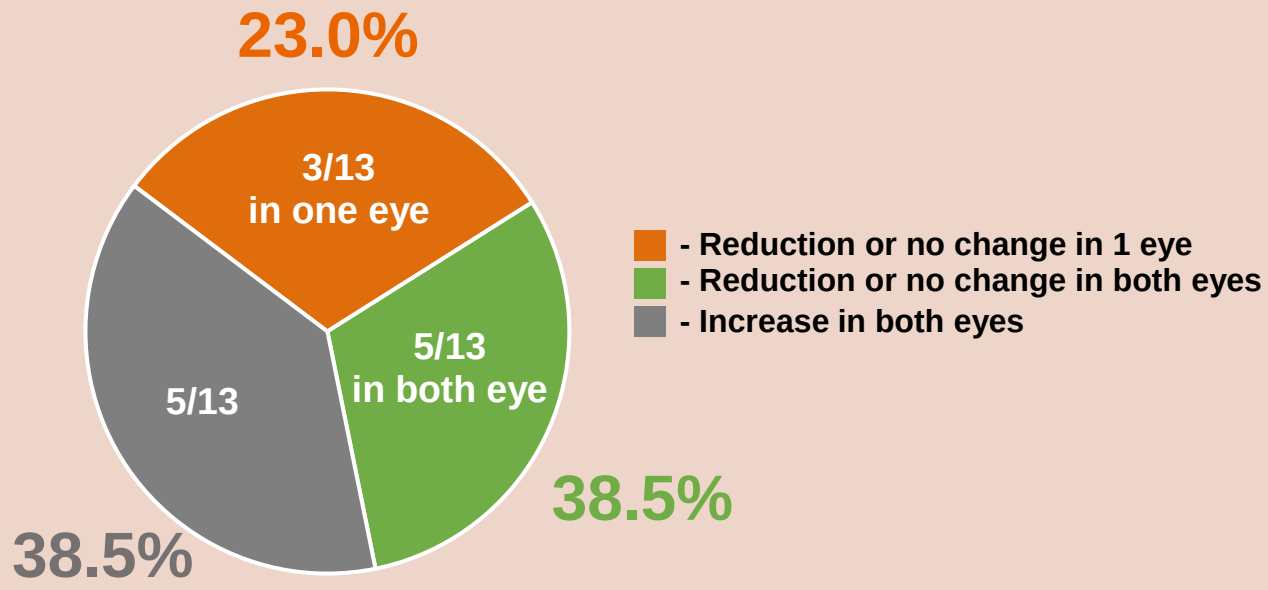
INTERIM PHASE 2 DATA: CHANGE IN QDAF IN ADOLESCENT STGD1 SUBJECTS



Areas of QDAF progressively evolve into ‘dead retina’.

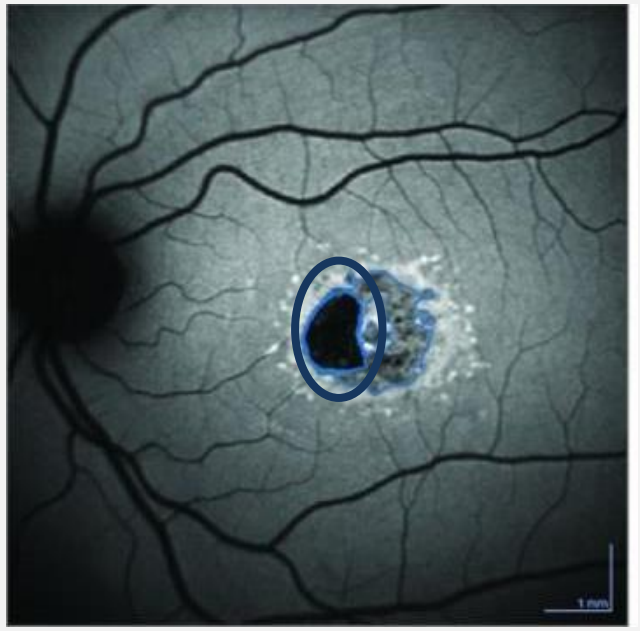
8 of 13 STGD1 patients showed a reduction or no change in QDAF

Distribution of Change in QDAF

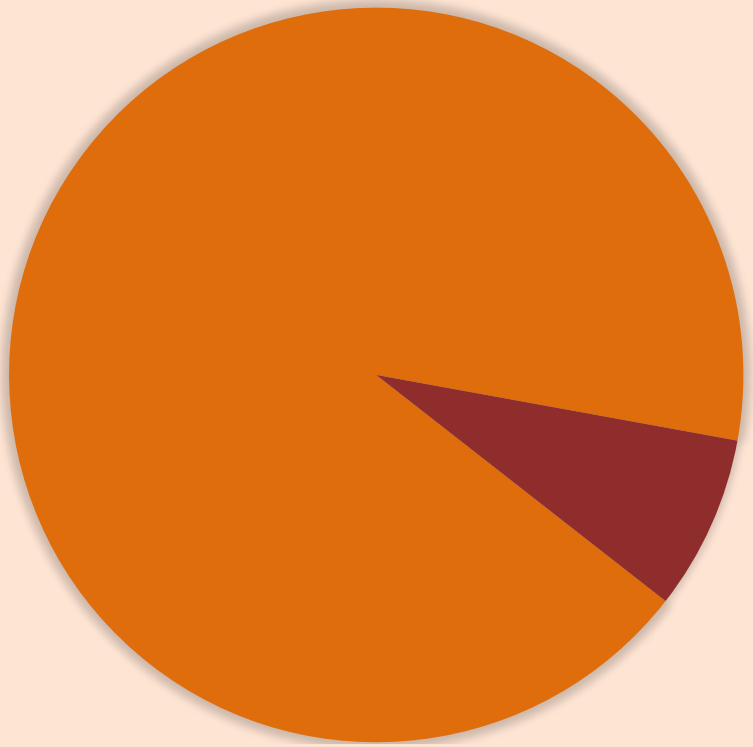


LBS 008

INTERIM PHASE 2 DATA: CHANGE IN DDAF IN ADOLESCENT STGD1 SUBJECTS



DDAF, or lesion (“dead retina”) in STGD1 patient as measured by retinal imaging. This is the area where retinal cells and vision are lost.



92.3%

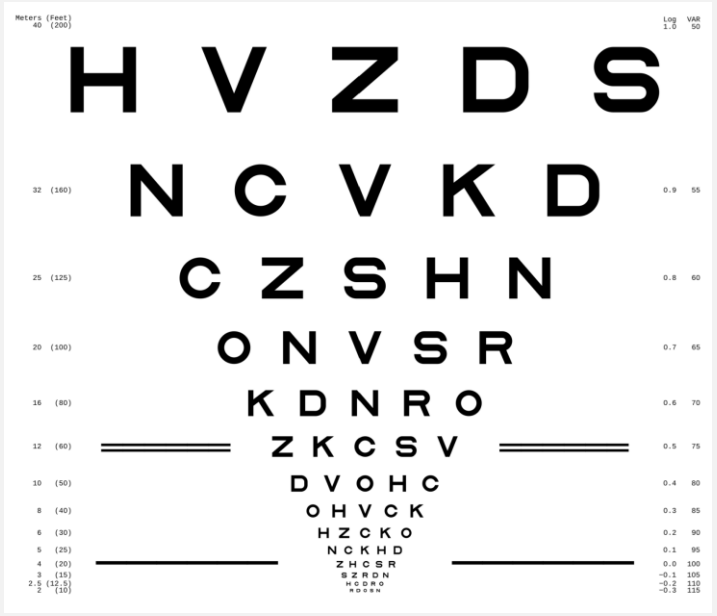
12 of 13 subjects showed no lesion growth

7.7%

1 of 13 subjects had lesion growth of 0.3 mm² in both eyes

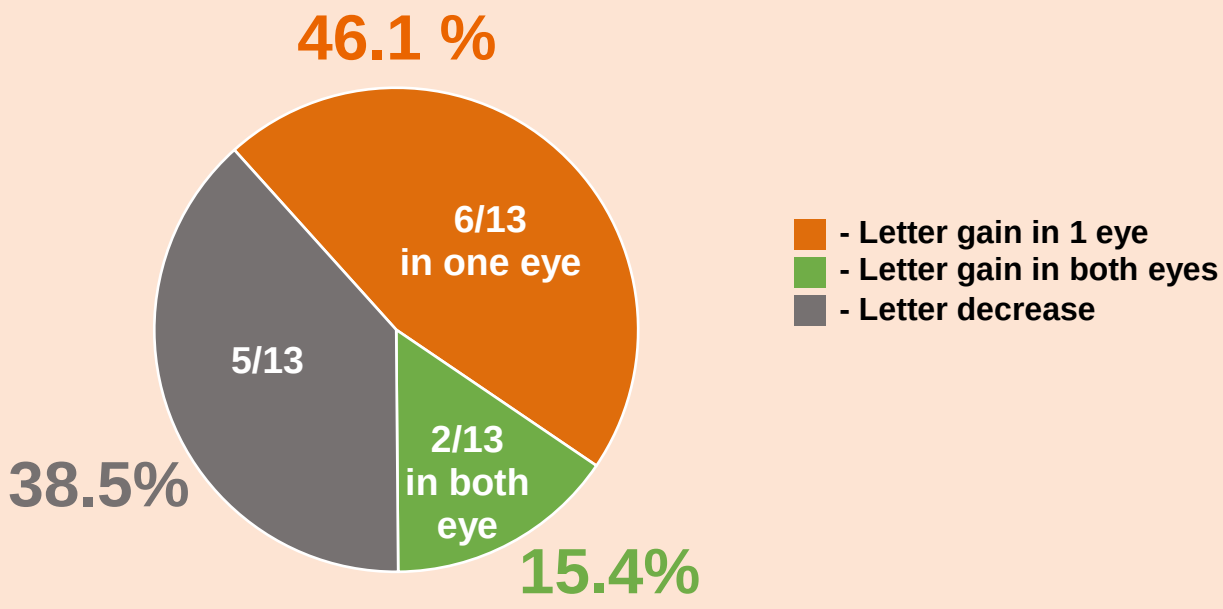
LBS 008

INTERIM PHASE 2 RESULTS: CHANGE OF VISION IN ADOLESCENT STGD1 SUBJECTS



Best-Corrected Visual Acuity (BCVA) Test
Provides letter score for each eye

Change in BCVA
BCVA gain in 8 of 13 Subjects (61.5%)



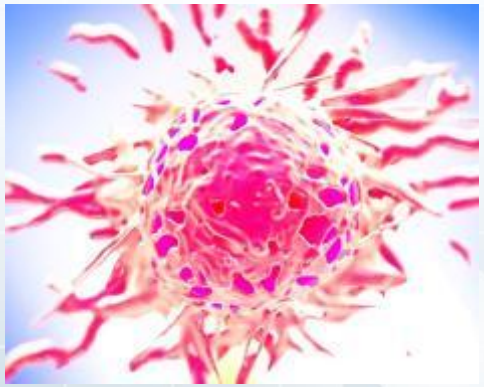
LBS-007
FOR BROAD VARIETY OF CANCERS

LBS 007

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

Non-ATP CDC7 Inhibitor

for treatment of Broad Variety of Cancer types



KEY OPPORTUNITY

Novel Anti-Cancer

Target Therapy

FDA ODD

for Acute Lymphoblastic Leukemia or ALL (US)

MARKET

$5B

Expected 2026 market size of AML & ALL

1.7 in 100k

Acute lymphoblastic leukemia (orphan disease)

$55B

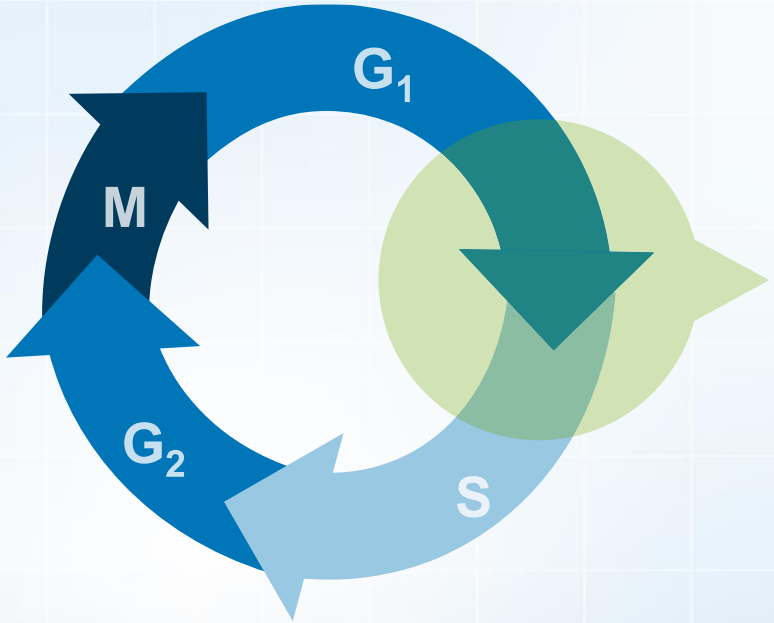
Expected 2023 market size of pancreatic, lung, ovarian cancers

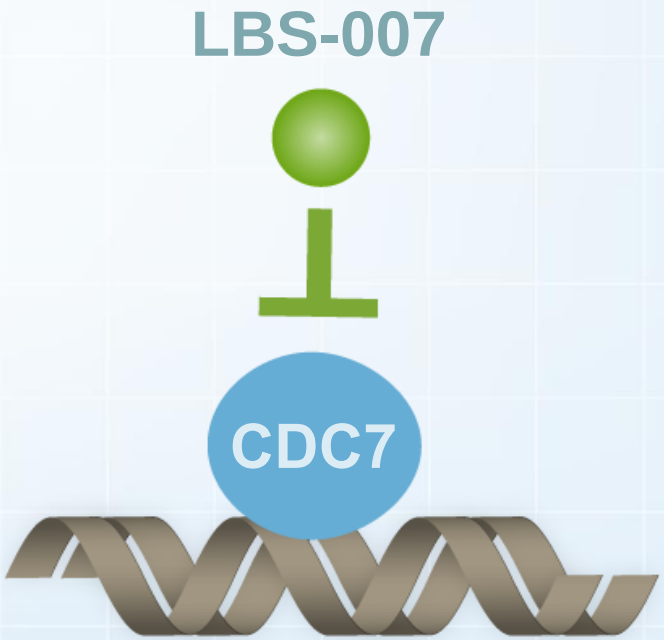
$6B

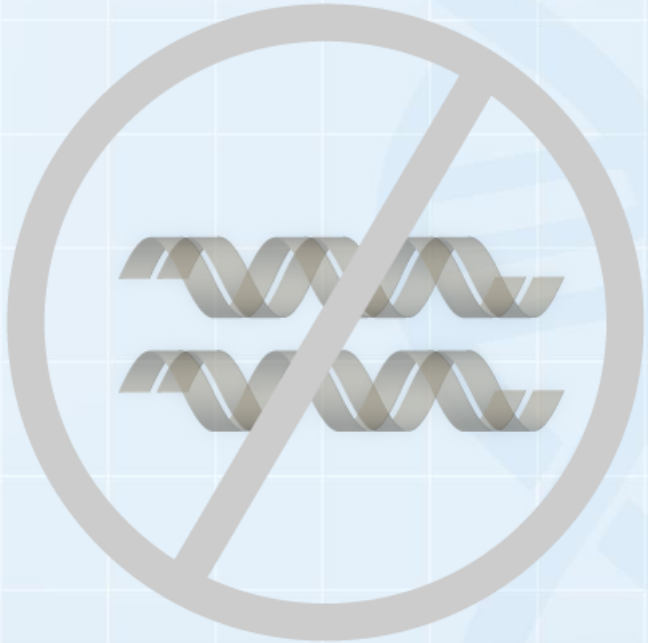
Estimated global market

Reference: Globaldata, Marketwatch, NIH National Cancer Institute

Inhibits CDC7 in Cell Cycle Regulation







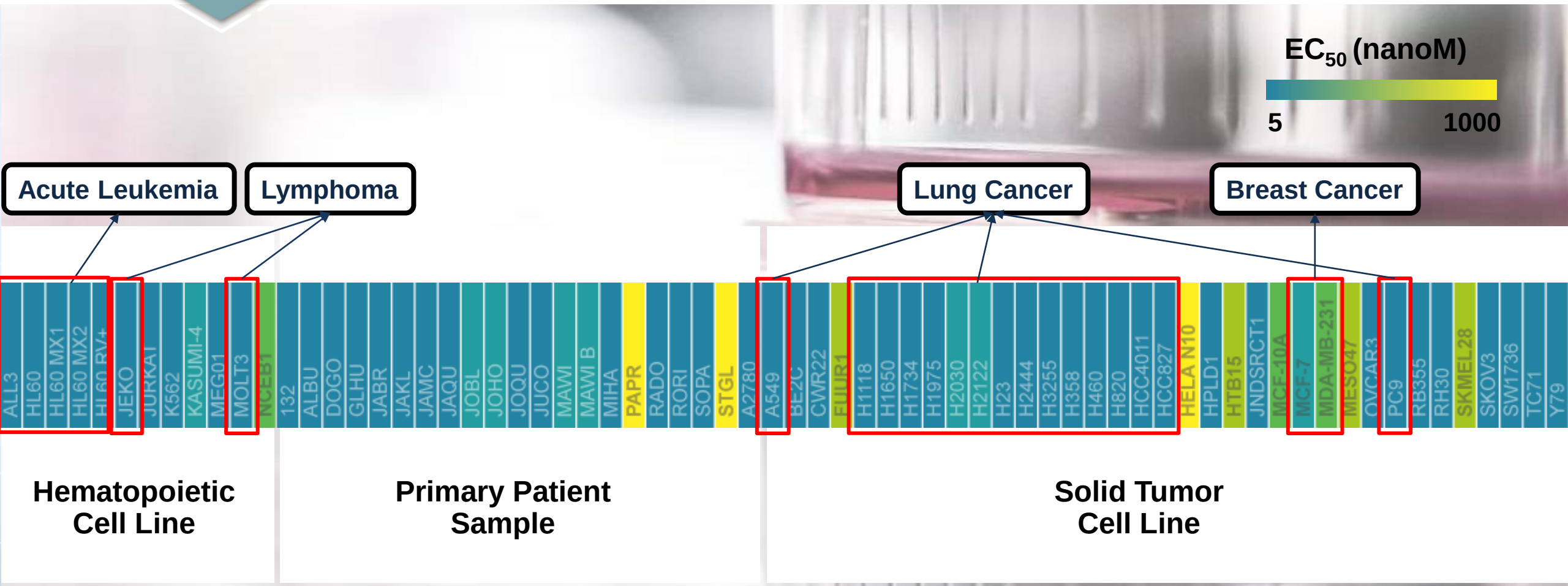
1 TARGETS
S Phase Progression

2 INHIBITS
CDC7's role in
DNA Replication

3 PREVENTS
Cell Division

LBS 007

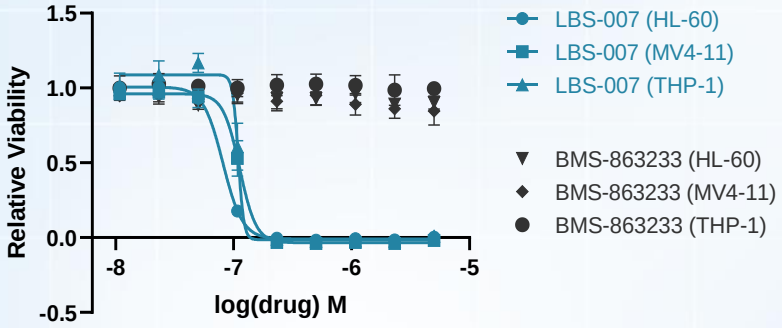
Potently Inhibits Multiple Cancer Cell Lines & Primary Patient Samples of Blood Cancers



SUPERIOR EFFICACY AT NANOMOLAR POTENCY

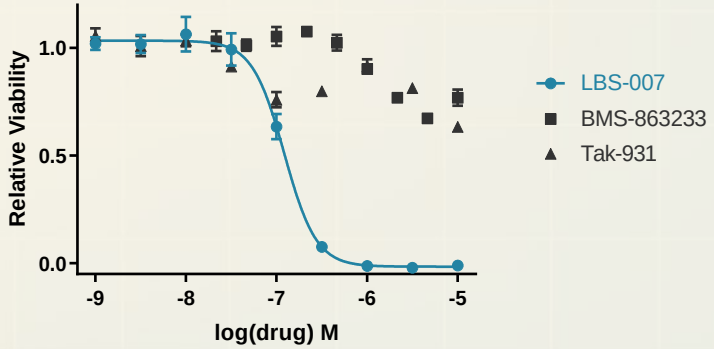
Approx. 0.15μ molar of LBS-007 can achieve therapeutic effect on cancer cells

AML



EC_{50} (nM)	HL-60	MV4-11	THP-1
LBS-007	**83.8**	**71.5**	**108**
BMS-863233	> 10,000	5,400	> 10,000

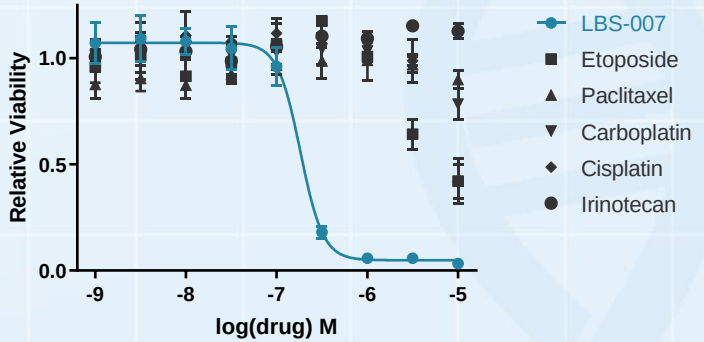
Pancreatic cancer



EC_{50} (nM)	Panc-1
LBS-007	**127**
BMS-863233	1,100
Tak-931	> 10,000

8.6x efficacy

Lung cancer



EC_{50} (nM)	H146
LBS-007	183
Cisplatin	2,800
Etoposide	> 10,000
Irinotecan	> 10,000
Paclitaxel	> 10,000
Carboplatin	> 10,000

15x efficacy

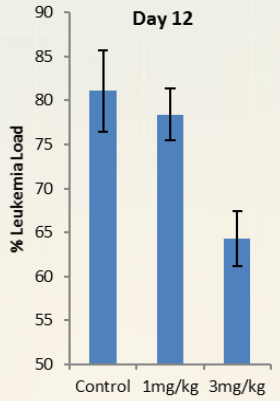
50+x efficacy

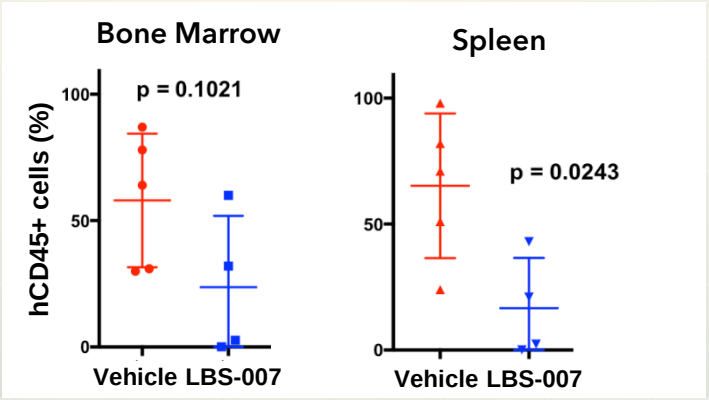
LBS 007

IN VIVO EFFICACY DEMONSTRATED IN ANIMAL MODELS

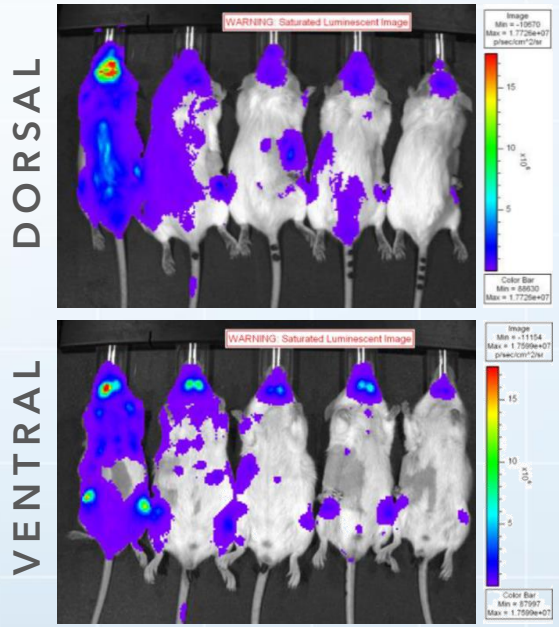
Potent tumor reduction in various cancer mouse models

AML



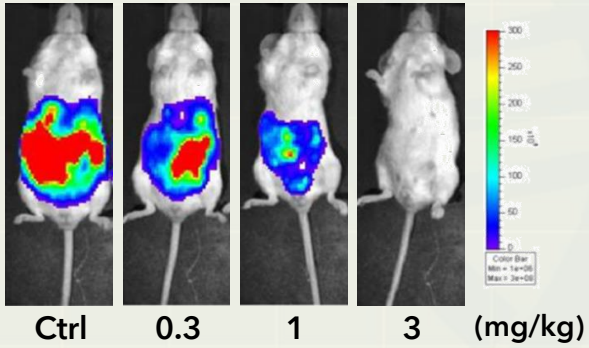


ALL

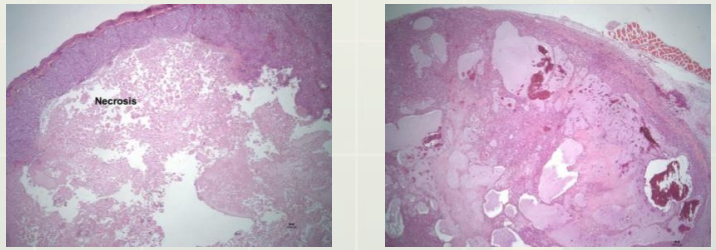


✓ Up to 95% tumor reduction

Ovarian cancer



Xenograft in mice



Lin BioScience

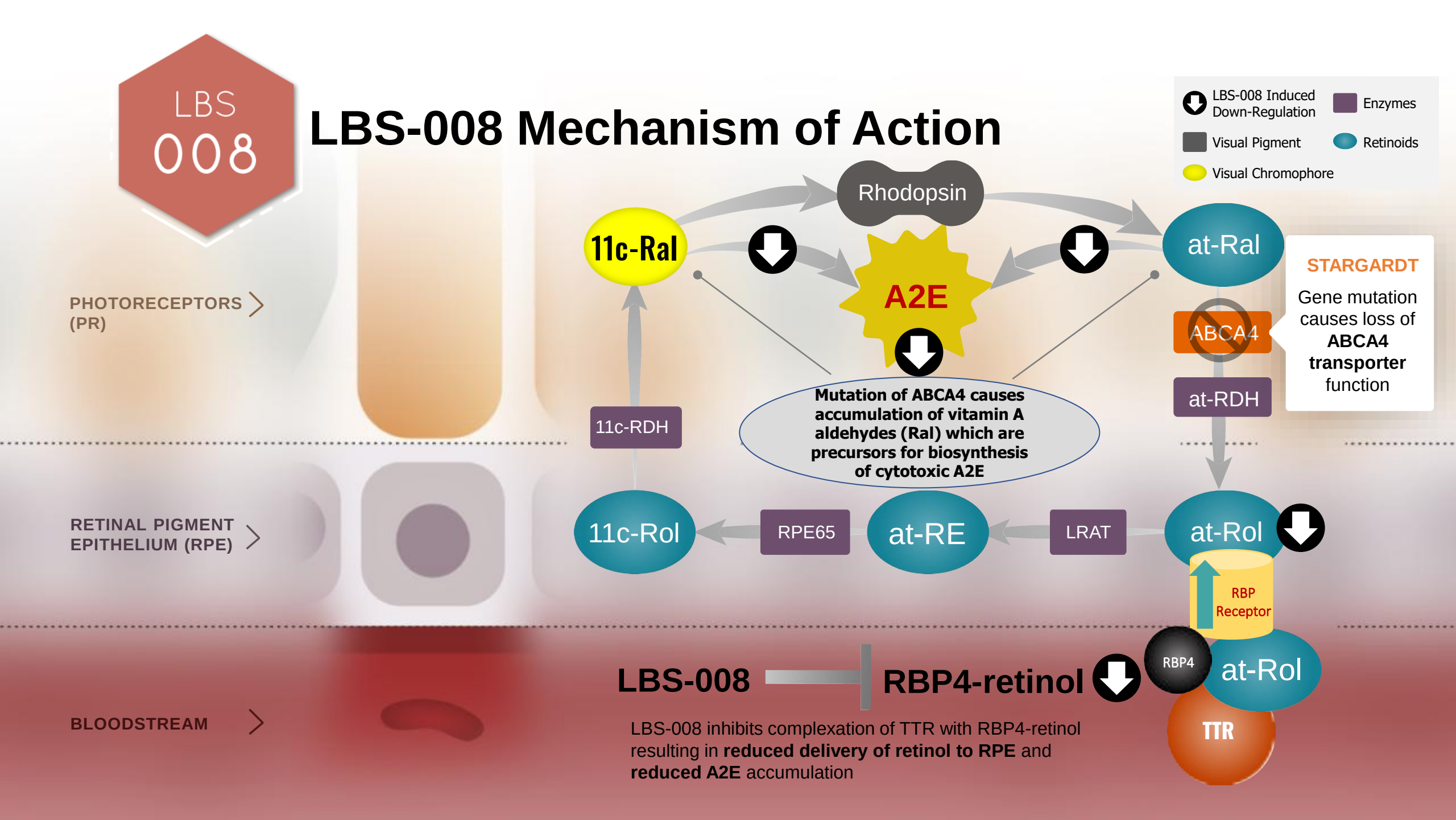
Bringing Hope to
Incurable Disease

info@linbioscience.com

APPENDIX

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

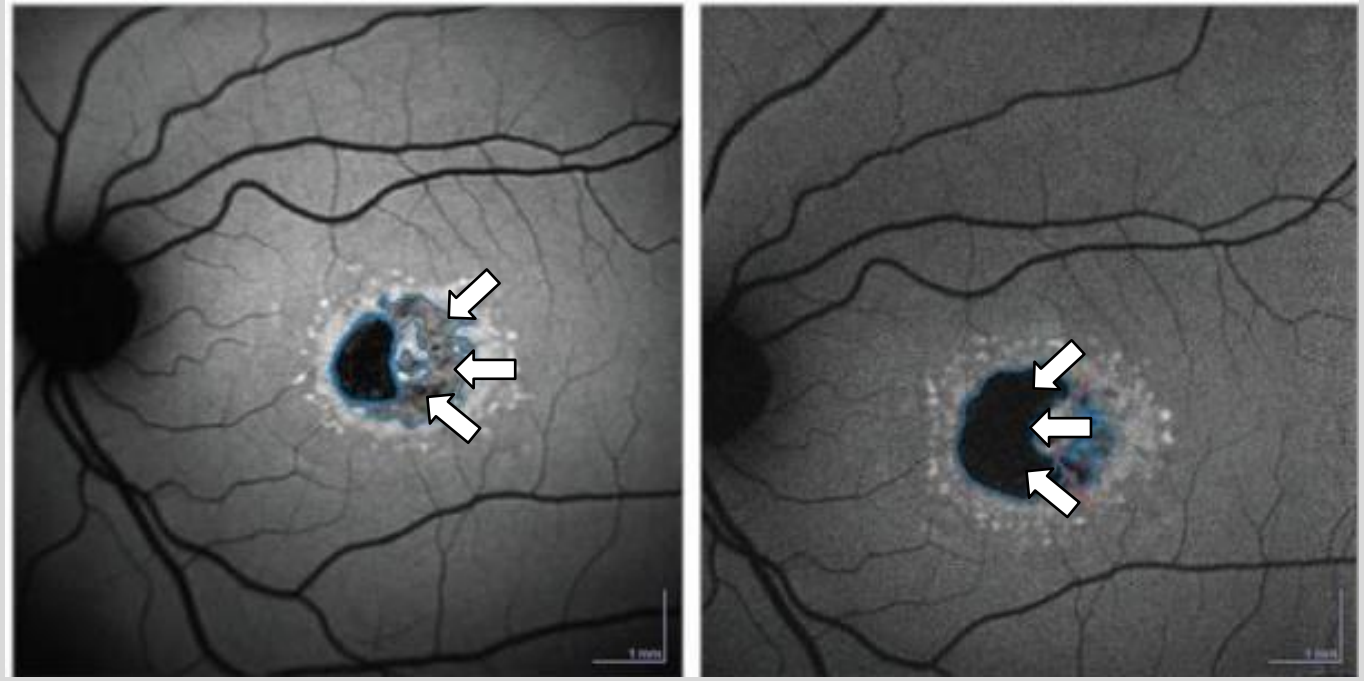
Pathogenesis of STGD1

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



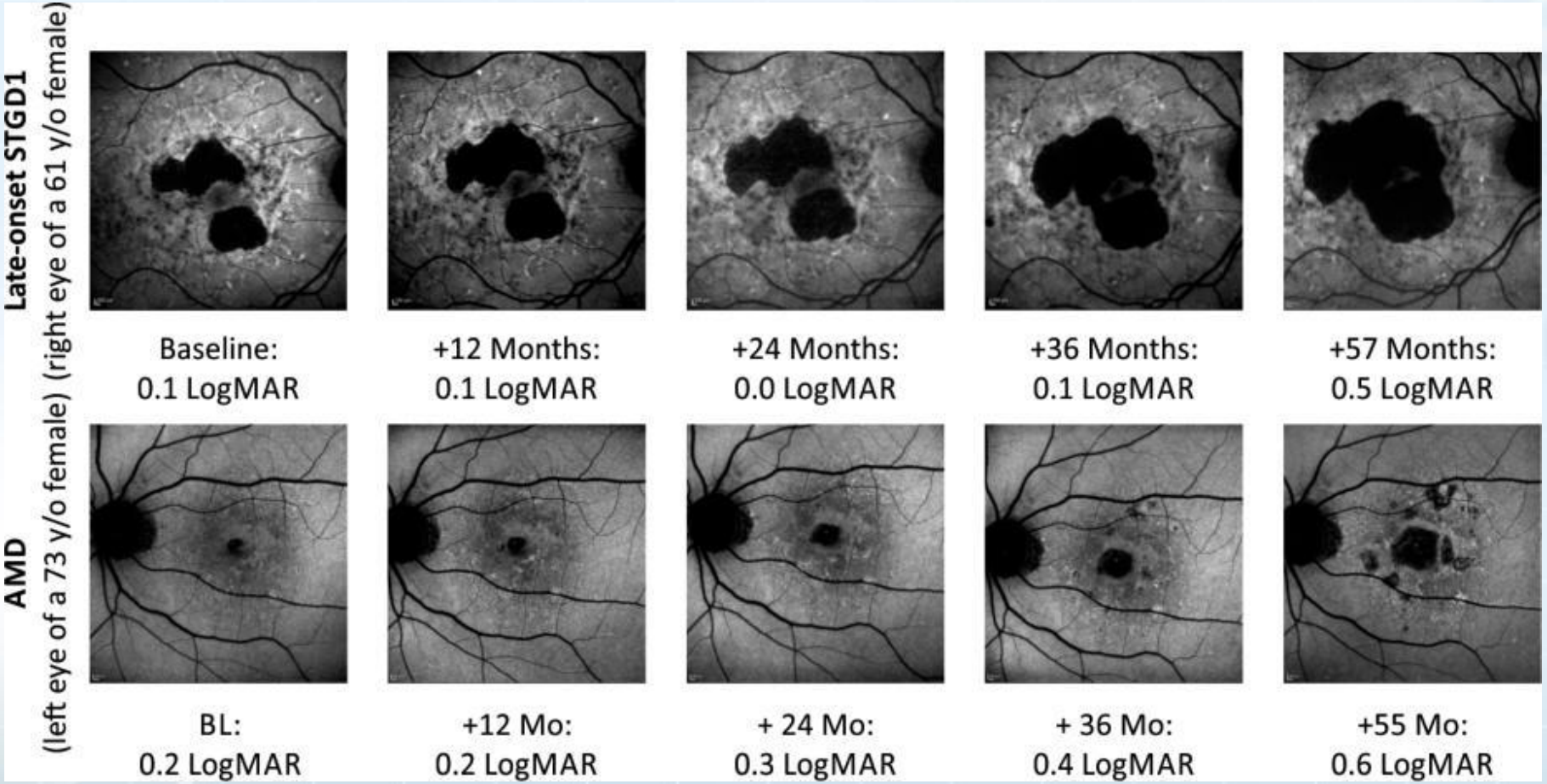
- The arrows point to areas of questionably decreased autofluorescence (QDAF) into which the central lesion advances.

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

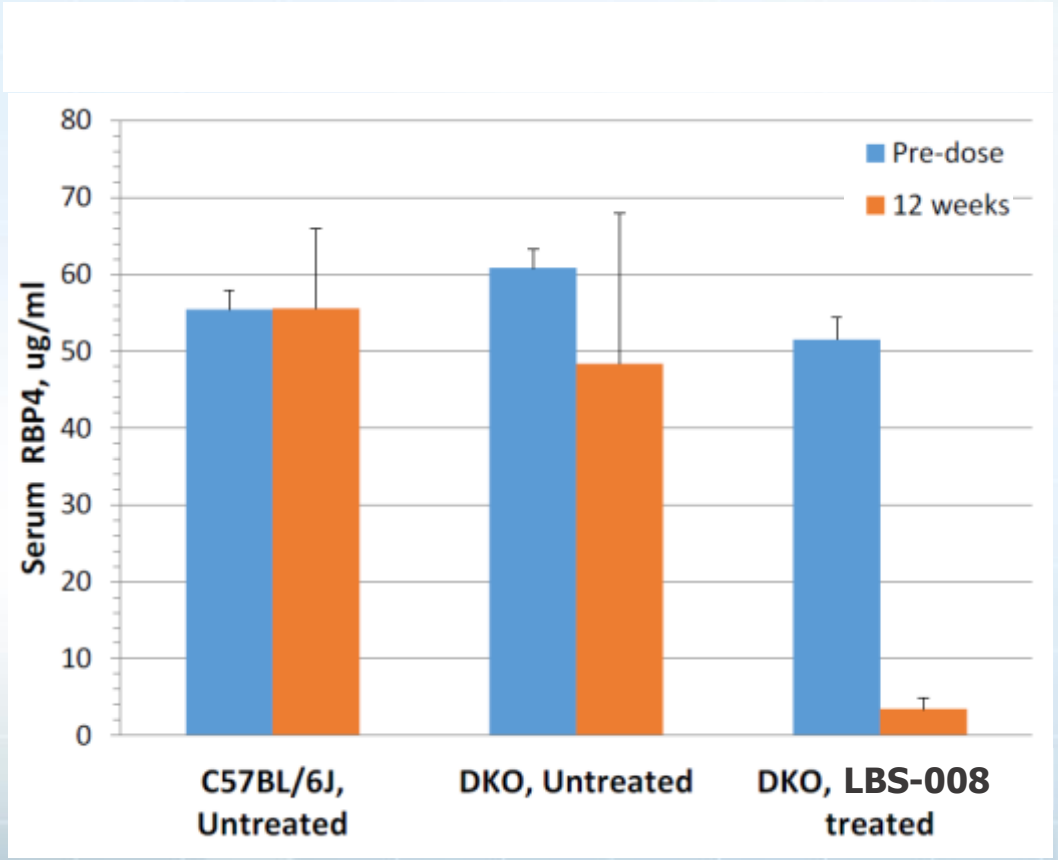


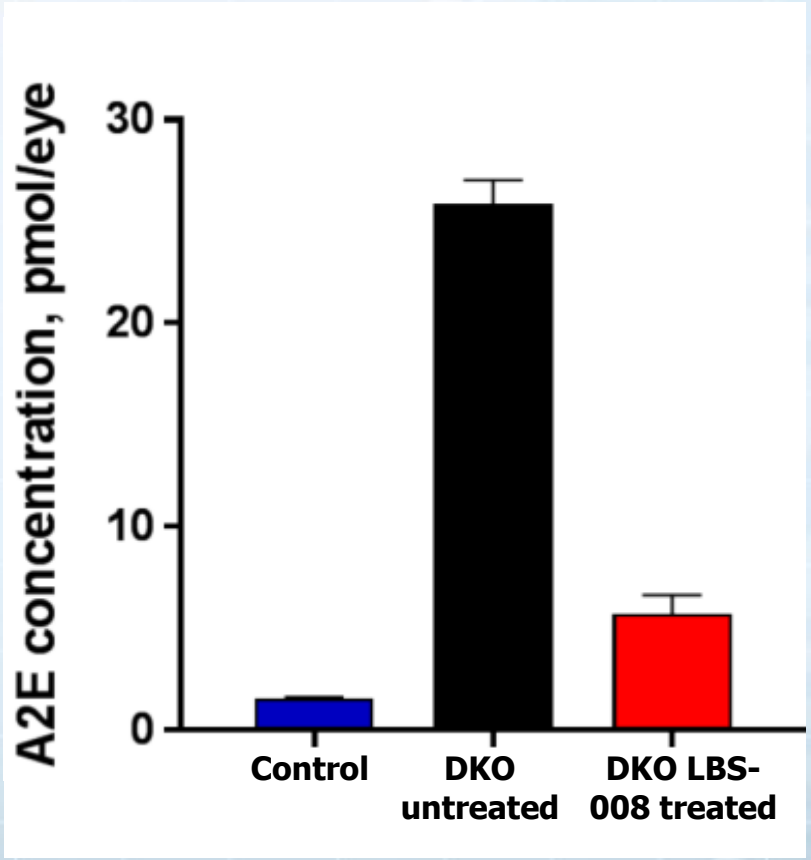
Reference: Lindner et al. Differential Disease Progression in Atrophic Age-Related Macular Degeneration and Late-Onset Stargardt Disease. Invest Ophthalmol Vis Sci. 2017;58(2):1001-1007.

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**