



# Nucorion Pharmaceuticals, Inc.

## *Introduction*

# Nucorion Overview

## *Innovation Focused on the Chinese Market*

- US-based company focused on treatments for **liver-related diseases in China**
- Founded in 2015, with technologies from Ligand Pharmaceuticals (Nasdaq: LGND) and contributions from a faculty member of The Ohio State University
  - There is an established heritage of **successful companies based on Ligand technologies** (Retrophin and Viking Therapeutics)
  - Active involvement from scientific advisors that include **world-renowned leaders** in fields of drug discovery and delivery
- Series A funding of \$5 m (July 2016) has yielded **promising preclinical proof-of-concept data** for Nucorion's lead programs
  - Silver River International Investments Ltd. and Ligand invested in the Series A
  - Efficient operation has allowed substantial progress with minimal cash burn
- First part Series B funding of \$5 m (July 2019) designated for US phase 1 clinical development of hepatitis B program
  - Ji-Bao pharmaceuticals and Ligand participated
  - Ji-Bao licensed China rights of the hep-B lead compound and responsible for the clinical development in China
- Seeking additional **\$10 million** in Series B funding to obtain clinical proof-of-concept for the second program



# Liver Diseases in China

## A Growing Epidemic



- Due to economic growth, lifestyle/environmental changes, national policies and an aging population, China is the **fastest growing** pharmaceutical market among emerging countries<sup>1</sup>
- The liver-related markets that Nucorion's pipeline is addressing are currently at \$2 b USD, and are **expected to double** to nearly \$4 b by 2024<sup>2</sup>
- Liver diseases in China are poised to create a **global healthcare burden**.  
Key market facts<sup>3</sup>:
  - **~300 million people** are affected by liver diseases in China
  - Liver cancer is **second most common cause of death** in China
  - China accounts for **over half** of liver cancer deaths worldwide
  - Hepatitis B carrier rate in China **now approaching 10%** of population (compared to <1% in US and EU)<sup>4</sup>

<sup>1</sup> Ni, et al. *Globalization and Health*, 2017, 31:21

<sup>2</sup> Global Data, *Pharma Intelligence*, 2018

<sup>3</sup> Wang, et al. *Hepatology*, 2014, 2099-2108

<sup>4</sup> Yan, et al. *J. Clin. Translational Hepatology*, 2014, 15-22

# Nucorion Overview

## *Cutting-edge LTP™ Technology*

- Proprietary liver-targeting prodrug (LTP) technology to generate *best-in-class* novel medicines by **activating drugs in the liver**
  - Technology is designed to increase liver concentration of actives to maximize efficacy and/or potency at site of interest
  - Also reduces drug exposure outside of liver, minimizing side-effects
- Licensed for Nucorion programs from Ligand Pharmaceuticals
- Recent data has demonstrated **clear preclinical superiority** over ProTide technology used in Sovaldi® and VEMSIDY® (Gilead), and Acelarin (NuCana)
  - Data presented at *EASL's International Liver Conference, April 14, 2018*



# Nucorion Overview

## *Scientific Advisory Board*

- Nucorion benefits from the active involvement from scientific advisors that include **world-renowned leaders** in fields of drug discovery and delivery



***Stephen Benkovic, Ph.D.***

- National Medal of Science recipient (2010)
- Penn State University (Professor/Chair of Chemistry)
- National Academy of Science member
- Anacor Pharmaceuticals Co-Founder



***Jack Szostak, Ph.D.***

- Nobel Laureate (2009 Nobel Prize for Medicine)
- Harvard Medical School (Professor of Genetics)
- Howard Hughes Medical Institute (Investigator)
- Massachusetts General Hospital (Distinguished Investigator)
- National Academy of Science member



***John Kozarich, Ph.D.***

- Ligand Pharmaceuticals (Chairman); Scripps (adjunct professor)
- ActivX Biosciences (Chairman/President)
- Merck & Co. (Head of Research)
- University of Maryland and Yale University (Professor)



***Lin Zhi, Ph.D.***

- Ligand Pharmaceuticals (VP, Chemistry)
- Over 25 years discovery & development experience
- Co-author of >60 publications
- Inventor on >100 issued patents
- Inventor of LTP™ Technology platform



***Zucai Suo, Ph.D. Co-Founder and Chair of Scientific Advisory Board***

- Florida State University
- The Ohio State University (Professor of Chemistry & Biochemistry)
- Harvard Medical School (Postdoctoral Fellow)
- Eli Lilly & Co



# Nucorion Overview

## *Robust, Lower-Risk Pipeline*

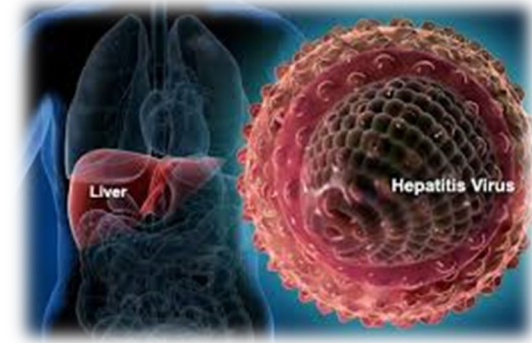
- Multiple **potential *best-in-class*** molecules for an array of liver-related indications
  - All are novel prodrugs of **clinically-validated** actives
  - Prodrug design **avoids off-target safety concerns**

Program Description	Lead Identification	Lead Optimization	Preclinical Development	Upcoming Development Events
<b>NCO-1010</b> <i>LTP-enabled Nucleotide Analog for Hepatitis B</i>				<ul style="list-style-type: none"><li>• IND/Phase 1a: 1H 2020</li><li>• Phase 1b: 2H 2020</li></ul>
<b>NCO-2020</b> <i>LTP-enabled agent for Hepatocellular Carcinoma</i>				<ul style="list-style-type: none"><li>• Clinical candidate selection: 3Q 2019</li><li>• IND: 3Q 2020</li><li>• Clinical POC: 2H 2021</li></ul>
<b>NCO-3030</b> <i>LTP-enabled agents for Solid Tumors</i>				<ul style="list-style-type: none"><li>• Clinical candidate selection: 2H 2019</li><li>• IND: TBD<sup>1</sup></li><li>• Clinical POC: TBD<sup>2</sup></li></ul>

<sup>1</sup> TBD if the candidate compound distinct from NCO-2020

<sup>2</sup> Depending upon funding availability

# HBV Opportunity



- Established, multi-billion dollar market dominated by Gilead
  - VEMLIDY® (TAF): only new HBV drug in a decade
  - Viread® (TDF) and VEMLIDY® - 2018 Gilead global sales of <\$3b<sup>1</sup>
- China situation analysis
  - Hepatitis B carrier rate in China **now approaching 10% of population<sup>2</sup>**
  - Viread® generic approved in 2017
  - Generic entecavir is the leading HBV drug
  - VEMLIDY® approved 4Q 2018
- Nucorion program (NCO-1010), potentially **best-in-class**
  - Potentially **10-fold more potent** than TAF
  - Potentially **>3-fold more liver-selective** than TAF
- Competitions landscape
  - multiple novel drugs in development, but no immediate success in sight
  - Combo regimen expected with multiple mechanisms, nucleotide-based drug is expected to be the core of treatment

<sup>1</sup> Gilead Q4 2018 Earnings Results Presentation  
<sup>2</sup> Yan, et al. *J. Clin. Translational Hepatology*, 2014, 15-22

# HCC Opportunity



- Market approaching a billion USD for small molecule drugs (~\$700m in 2017)<sup>1</sup>
  - Market leaders are Nexavar® (sorafenib) and Stivarga® (regorafenib), approved in 2017 for 2<sup>nd</sup> line HCC
  - No nucleotide-based drug approved for HCC
- China situation analysis
  - Liver cancer is **second most common cause of death** in China<sup>3</sup> and treatment options limited
- Nucorion program – NCO-2020, potentially *first-in-class*
  - Oral delivery of a potent nucleotide agent to the liver to potentially replace the first line treatment of transartery chemoablation (TACE)
  - Lowered development and regulatory risks
- Competitive Landscape
  - New kinase inhibitors approved in US and in China<sup>4</sup> second line with limited efficacy
  - Immuno-oncology (I-O) therapy; Opdivo (PD-L1 inhibitor) approved as second line
  - I-Os will boost market size, although response rate remains low

<sup>1</sup> Mordor Intelligence, Liver Cancer Market, 2017

<sup>2</sup> Bayer Annual Report 2017

<sup>3</sup> Wang, et al. *Hepatology*, 2014, 2099-2108

<sup>4</sup> Eisai Major R&D Pipeline, February 2, 2018



# Nucorion Overview

## *Current Status and Plans*

- Data obtained post Series A has **clearly validated** the LTP hypothesis
  - Preclinical research goals were achieved on time and under budget
- **Series B investment** will be focused on *Proof-of-Concept* in humans
  - Raising \$15 million from US and Asia-based investors (\$5 million completed)
  - Positioned to obtain **clinical proof-of-concept** data for two programs addressing billion dollar markets within two years from funding close

# Nucorion Overview

## *An Attractive Investment Thesis*

- Potential for a leverageable and **lower-risk drug development platform**
  - Enhancing efficacy and safety profile of validated actives to create *best-in-class* novel medicines for the Chinese market
- A **clear and rapid plan** to clinical *proof-of-concept*
  - Programs quickly approaching or at Clinical Candidate stage
  - Clinical trial designs based on protocols of previously-approved drugs
- **High potential return** for Series B investors
  - Novel, patentable drugs for validated targets, for growing markets with high unmet medical needs
  - Low operating cost structure focuses investment into value-driving events
  - Clinical proof-of-concept for two programs in less than 24 months
  - Potential IPO event in 30-36 months

