



NeuroBo
PHARMACEUTICALS

**Novel Treatments for
Neurodegenerative and
Cardiometabolic Conditions**

Multi-modal, disease-modifying therapies

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COMPANY OVERVIEW

Clinical-stage biopharmaceutical company with three drug programs to impact a range of indications in neurodegenerative and cardiometabolic disease

Multiple Drug Programs; One Phase 3-Ready

Multi-modal with potential to be disease-modifying

- **NB-01**: Phase 3 initiation H1 2020; targeting Painful Diabetic Neuropathy (PDN)
- **NB-02**: IND-ready; targeting Alzheimer's Disease (AD) and other dementias
- **Gemcabene**: 25 Phase 1 and Phase 2 trials completed. Awaiting FDA decision to start Phase 3

Large Therapeutic Markets with High Unmet Need

- **Painful Diabetic Neuropathy (PDN)**: affects 8.4M* people globally; current drugs have insufficient efficacy and are poorly tolerated
- **Alzheimer's disease (AD) & other dementias**: AD affects 27.3M* people globally; with no approved disease modifying therapies
- **Dyslipidemias including orphan and prevalent indications**: HoFH and SHTG globally affect 3,200* and 12.5M* respectively

Staged Financing Strategy with Experienced Team

- Combination of equity and partnering; **one Asian partnership signed (Beijing SL)**
- Experienced executive team in drug development, innovation, and corporate strategy
- Reverse merger completed with Gemphire Therapeutics (Nasdaq: GEMP) on December 30, 2019; **new NASDAQ listing (NRBO)**



PROVEN LEADERSHIP TEAM

Richard J. Kang, PhD
President & CEO

- Founder of JK BioPharma Solutions and senior management at companies including NeolImmuneTech in immuno-oncology
- Visiting Fellow at NIH and senior research experience in host-disease pathogen interactions

Mark Versavel, MD, PhD, MBA
Chief Medical Officer

- 30 years of drug development experience from Phase 1 to Phase 3 at Pfizer (Lyrica), Bayer, Sunovion (Aptiom, Lunesta)
- Leadership roles at 5 biotech companies
- Founder & President of vZenium LLC
- Drug approvals: 2 NDAs, 1 sNDA

Nikki Shannon, RegN, BA
VP, Clinical Operations

- 26 years of drug development experience from Phase 1 to Phase 4 at Solvay, Sanofi Pasteur, Vertex (Kalydeco), Cubist/Merck, AstraZeneca, Tetraphase (Eravacycline)
- Leadership roles at 4 pharma companies; >55 studies including 14 Phase 3
- Drug approvals: 2 NDAs, 2 MAAs

EXPERT SCIENTIFIC ADVISORY BOARDS

CHAIRMAN

Roy Freeman, M.D.
Expert in Peripheral Nerve Disorders and Neurodegenerative Diseases

- Professor of Neurology, Harvard Medical School
- Director of the Center for Autonomic and Peripheral Nerve Disorders

PAIN

Robert H. Dworkin, PhD
Leader in Neuropathic Pain Clinical Trials

- Professor of Anesthesiology, Neurology, Psychiatry, and Experimental Therapeutics at the University of Rochester School of Medicine
- Director of the Anesthesiology Clinical Research Center

Allan Basbaum, PhD, FRS
Leader in Pain Research

- Professor and Chair, Department of Anatomy, University of California San Francisco
- Former Editor-in-Chief of PAIN, the journal of the IASP

Bob Rappaport, M.D.
Regulatory Expert

- Former Division Director of Anesthesia, Analgesia and Addiction Products at the U.S. Food and Drug Administration
- President and owner of Analgesic Concepts LLC

ALZHEIMER'S DISEASE & OTHER DEMENTIAS

Brian Bacsikai, PhD
Expert in Alzheimer's Disease Research

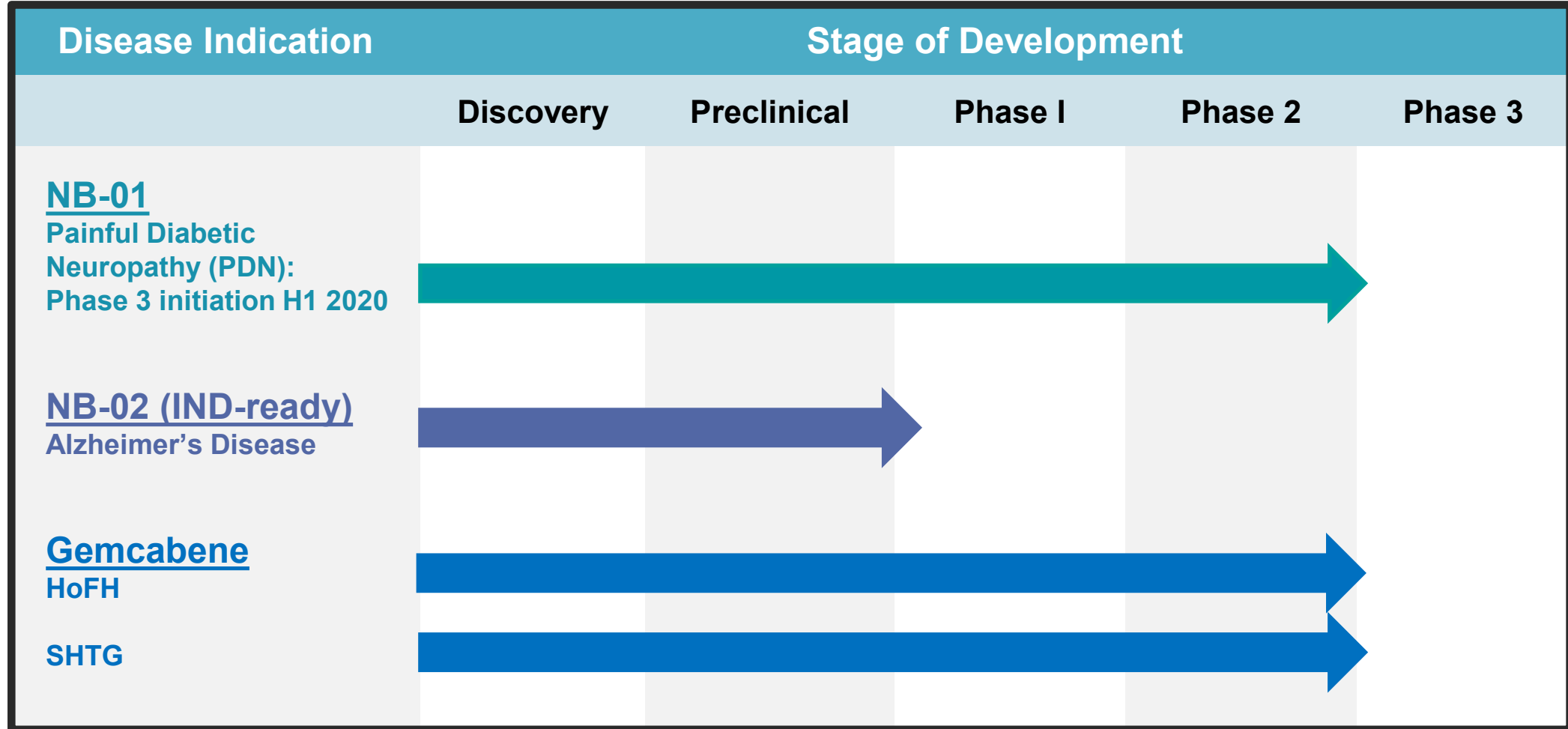
- Professor of Neurology, Harvard Medical School
- Principal Investigator, Neurology, Massachusetts General Hospital

Pierre N. Tariot, M.D.
Award-Winning Leader in Dementia

- Director, Banner Alzheimer's Institute, Arizona
- Research Professor of Psychiatry, University of Arizona College of Medicine



NEUROBO DEVELOPMENT PIPELINE



HoFH = Homozygous Familial Hypercholesterolemia
SHTG = Severe Hypertriglyceridemia



NB-01

Targeting neuropathic pain

First indication: PDN



PAINFUL DIABETIC NEUROPATHY OVERVIEW


- **Diabetes** is among the leading causes of neuropathic pain
 - A disorder known as painful diabetic neuropathy (PDN)
- PDN affects **8.4M** people worldwide representing global drug sales of **\$3.56B** (2018, *GlobalData*)
- **Pain can be severe** and debilitating, impairing sleep, limiting mobility, and **interfering with quality of life** (*Pop-Busui R et al., 2017*)
- Currently approved therapies have **limited efficacy**
 - **Less than 50%** of treated patients have a 50% response rate
 - **Adverse events** are common
 - Limits tolerability and adherence
 - **Limited success** with first and second-line drugs leading to **high frequency opioid use**
 - 14% and 19% of patient encounters involving gabapentin and pregabalin respectively also involved opioids (*FDA In Brief, 2019*)




FDA WARNING ON GABAPENTINOIDS FOR SERIOUS BREATHING PROBLEMS

 An official website of the United States government [Here's how you know](#) 



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FDA warns about serious breathing problems with seizure and nerve pain medicines gabapentin (Neurontin, Gralise, Horizant) and pregabalin (Lyrical, Lyrical CR)

When used with CNS depressants or in patients with lung problems

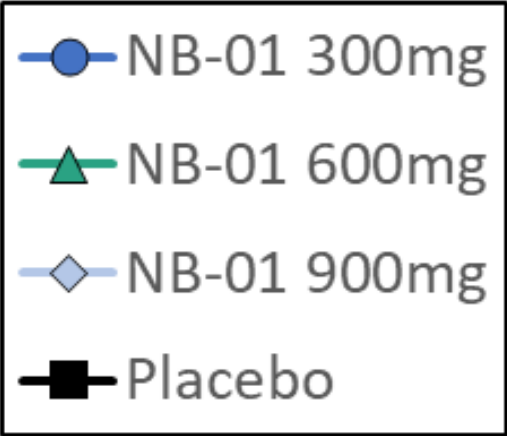
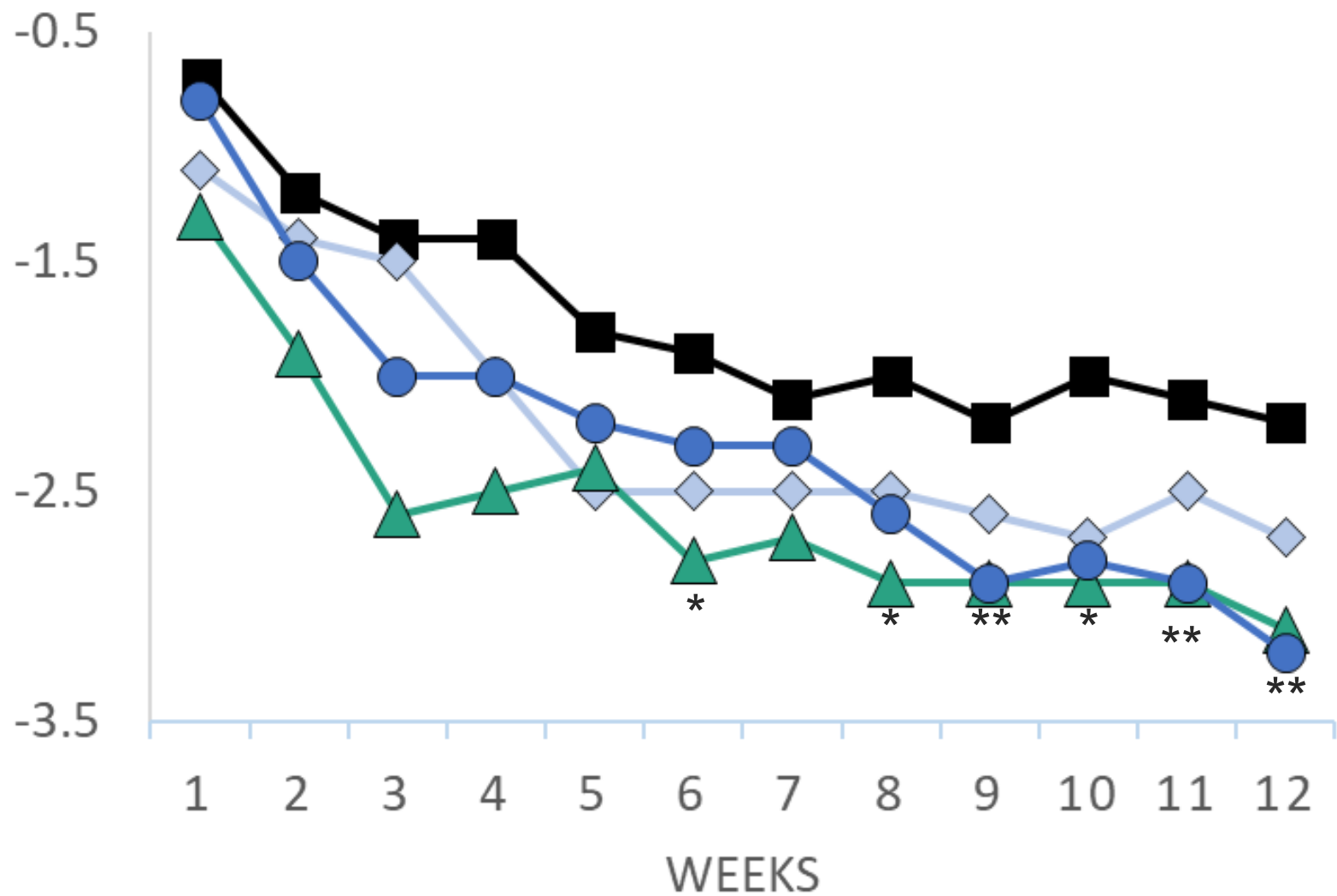
What is FDA doing?



We are requiring new warnings about the risk of respiratory depression to be added to the prescribing information of the gabapentinoids. **We have also required the drug manufacturers to conduct clinical trials to further evaluate their abuse potential, particularly in combination with opioids, because misuse and abuse of these products together is increasing, and co-use may increase the risk of respiratory depression.** Special attention will be paid to the respiratory depressant effects during this abuse potential evaluation.



NB-01 DEMONSTRATED PAIN REDUCTION IN US PHASE 2 STUDY



Reduction from Baseline in NRS Score

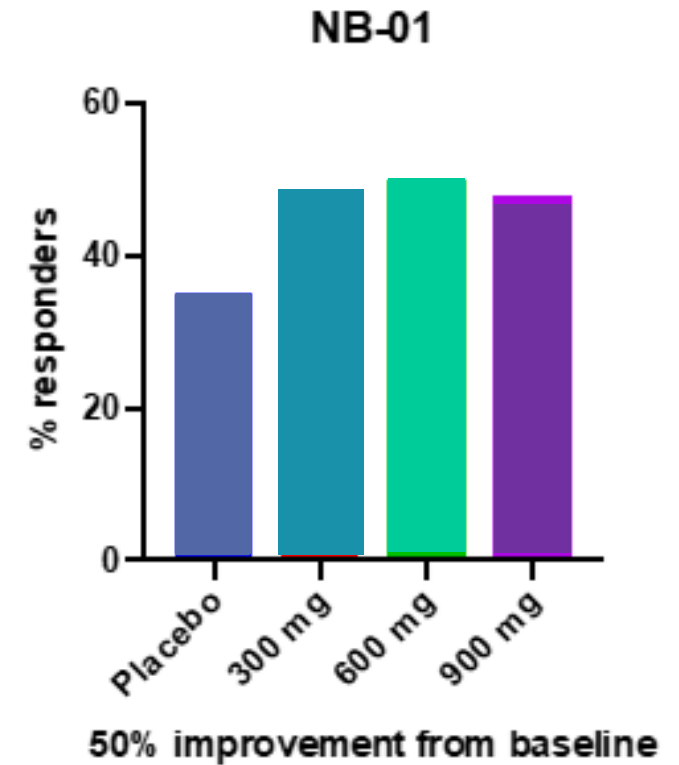
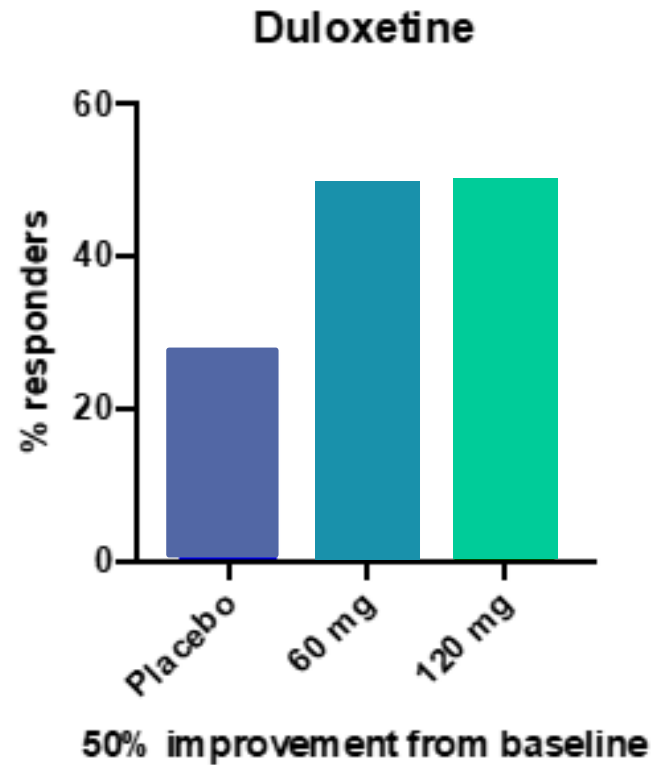
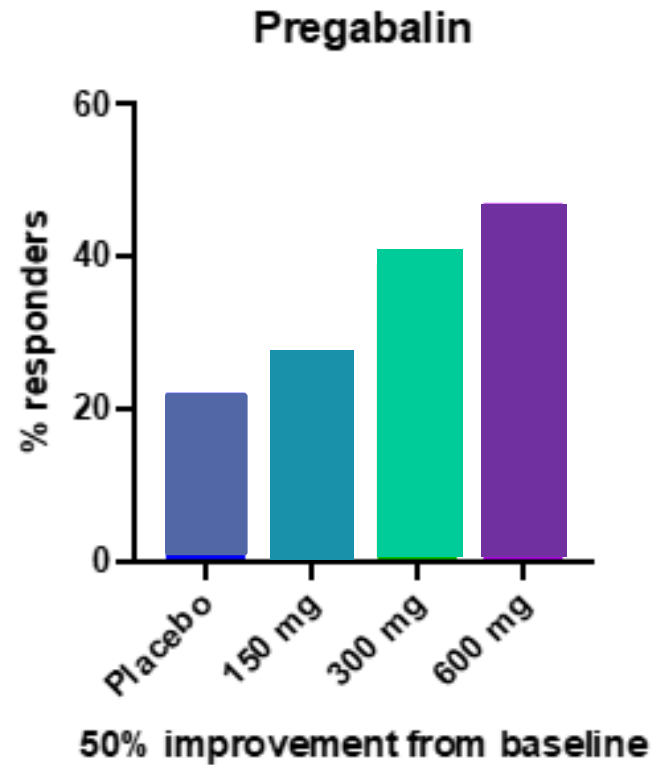
NRS: 11-point numeric rating
P values = change from baseline:
scale* <0.05, ** <0.01

ClinicalTrials.gov NCT01822925

14 US sites, 128 subjects, 3 doses vs. placebo



50% RESPONSE RATES - COMPARISON OF NB-01 TO APPROVED THERAPIES



ADVERSE EVENTS WITH NB-01 TREATMENT WERE SIMILAR TO PLACEBO

TEAEs with a ≥2% Difference (Safety Population)

	Incident on NB-01 N=96	Incident on Placebo N=32	Difference in Incident NB-01 from Placebo
Constipation	5.2%	0.0%	5.2%
Sinusitis	5.2%	0.0%	5.2%
Back pain	6.3%	3.1%	3.1%
Myalgia	3.1%	0.0%	3.1%
Pain in extremity	3.1%	0.0%	3.1%
Arthralgia	5.2%	3.1%	2.1%
Musculoskeletal pain	2.1%	0.0%	2.1%
Nasopharyngitis	2.1%	0.0%	2.1%
Pneumonia	2.1%	0.0%	2.1%

Duloxetine* (Placebo vs 60mg QD/BID)

- Nausea: 8% vs 24-27%
- Somnolence: 4% vs 15-20%
- Dizziness: 5% vs 10-13%

Pregabalin** (Placebo vs 300/600mg QD)

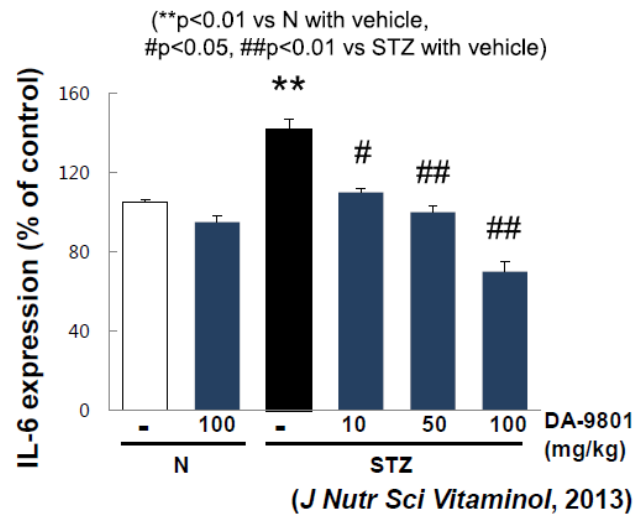
- Dizziness: 5% vs 23-28%
- Peripheral Edema: 7% vs 10-16%
- Somnolence: 3% vs 13-14%



DISTINCT MULTI-TARGET APPROACH: PRE-CLINICAL DATA

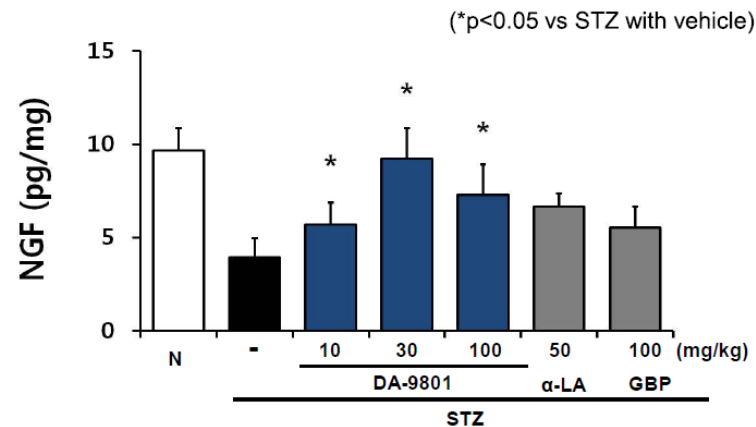
Anti-inflammatory

Reduction IL-6 Expression in STZ model



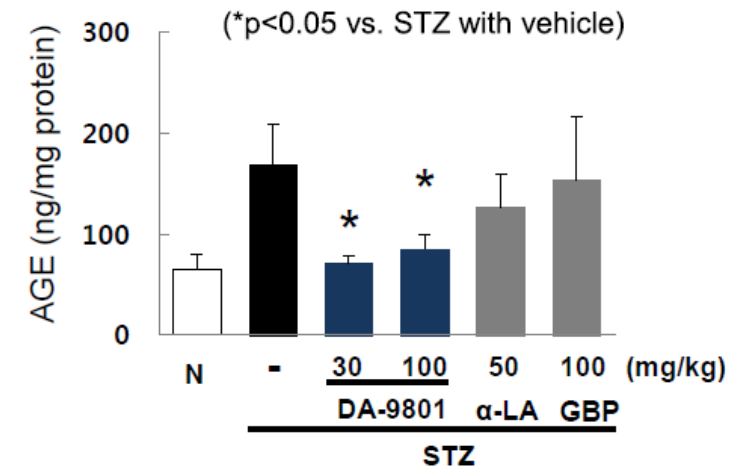
Nerve growth and repair

NGF restored to normal endogenous levels in STZ model



Reducing cell damage

AGE Reduction in STZ model



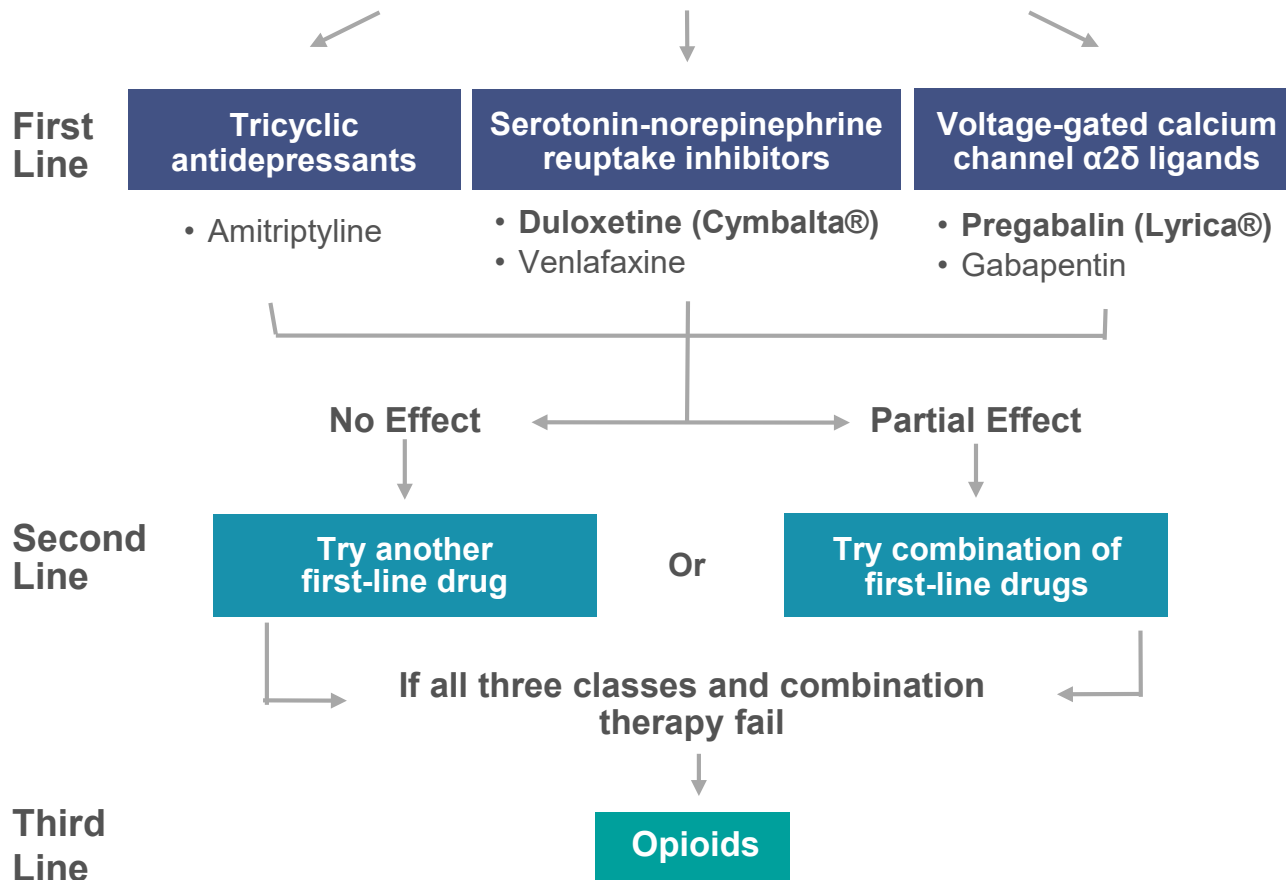
* Preclinical rodent models have also shown improved nerve conduction velocity (NCV), neurite outgrowth, and reduction of thermal and mechanical hyperalgesia



PDN TREATMENT PARADIGM



Confirmed painful diabetic neuropathy



Source: Adapted from Callahan et al., 2012

- PDN is a **multi-billion-dollar market** in U.S.
 - 2018 Lyrica® sales for PDN were \$1.87B*
- Available treatments **do not provide adequate relief** and have serious side effects
- Many **PDN patients resort to opioids** for pain management, which creates unwanted risk for addiction while treating a chronic condition
- In Phase 2 trials, **NB-01** demonstrated efficacy similar to results seen in studies of best-in-class approved drugs with **substantially fewer side effects**
- NB-01 may potentially demonstrate **disease-modifying properties**

*Source: GlobalData



PHASE 3 PDN TRIAL

Double-Blind, Placebo-Controlled; Safety, Efficacy, & Tolerability



- ~460 adults aged 18-75 years
- 6 months – 10 years hx PDN with \geq moderate pain
- 1 non-opioid concomitant medication allowed
- Daily patient reported pain scores (PI-NRS)
- PROs
- Placebo response mitigation design
- Dosing compliance monitoring

Placebo orally TID

NB-01 200mg orally TID
(600mg/day)

13 Weeks

Primary Endpoint:

- Change from baseline in weekly mean of daily average pain score

Secondary Endpoints:

- Responders on Patient Global Impression of Change
- Responders on PI-NRS
- Change from baseline in weekly mean of Daily Sleep Interference Scale

Conducted in U.S. only



NB-02

Targeting Alzheimer's disease &
Tauopathies



ALZHEIMER'S DISEASE & OTHER DEMENTIAS

Alzheimer's disease

- Alzheimer's disease (AD) affects **27.3M people** globally (2018, Global Data)
- Approved treatments **focus on symptomatic** management and largely on acetylcholinesterase (AChE) inhibition

Other Dementias

- **>20 diseases** that result from **tau protein aggregation** in the brain; progressive supranuclear palsy (PSP) is a key focus
- **No approved therapies** for patients with tauopathies

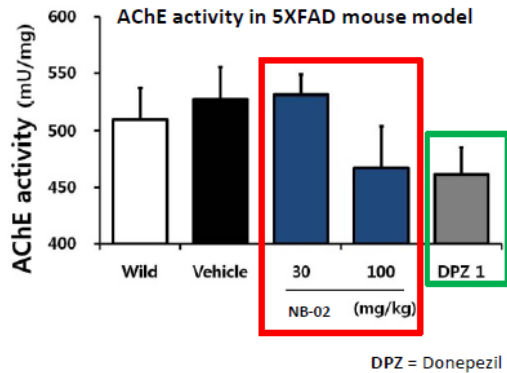
Significant opportunity for safe, disease-modifying therapies that restore cognitive function



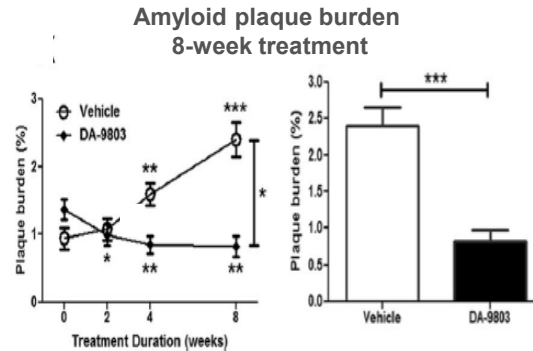
NB-02: OUR DISTINCT, MULTIPLE PATHWAY APPROACH

- Alzheimer's disease is a multi-mechanism disease with a complex pathophysiology
- NB-02 has effects on multiple pathways shown in pre-clinical models

**Inhibits
Acetylcholinesterase
(AChE)**

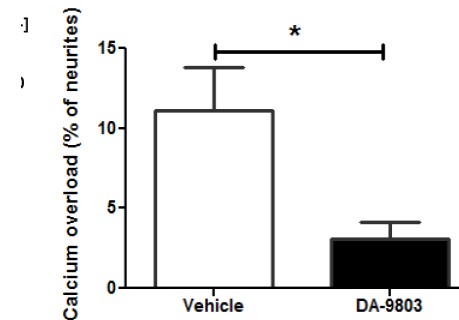


**Prevents Amyloid- β
Plaque Deposition**



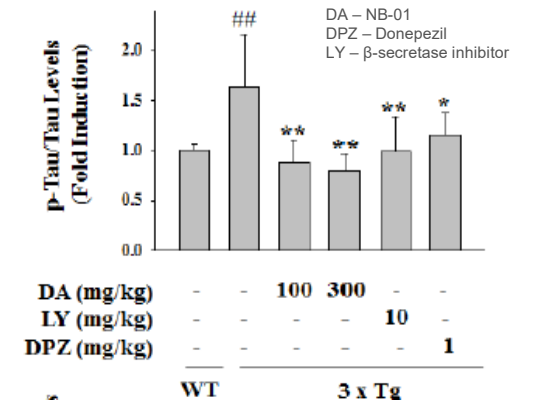
DA-9803 is NB-02
Pagnier et al., 2018
Alzheimer Research
& Therapy

**Restores Disrupted
Ca⁺⁺ Homeostasis**



DA-9803 is NB-02
Pagnier et al., 2018
Alzheimer Research
& Therapy

**Inhibits
Tau Phosphorylation**



IND-READY: EXTENSIVE PRECLINICAL STUDIES



NB-02 impacts multiple pathways implicated in neurodegenerative disease



Efficacy demonstrated in extensive cognitive and behavioral studies

Y-Maze, Morris Water Maze, and Novel Object Recognition studies show improved cognitive endpoints in transgenic mouse models



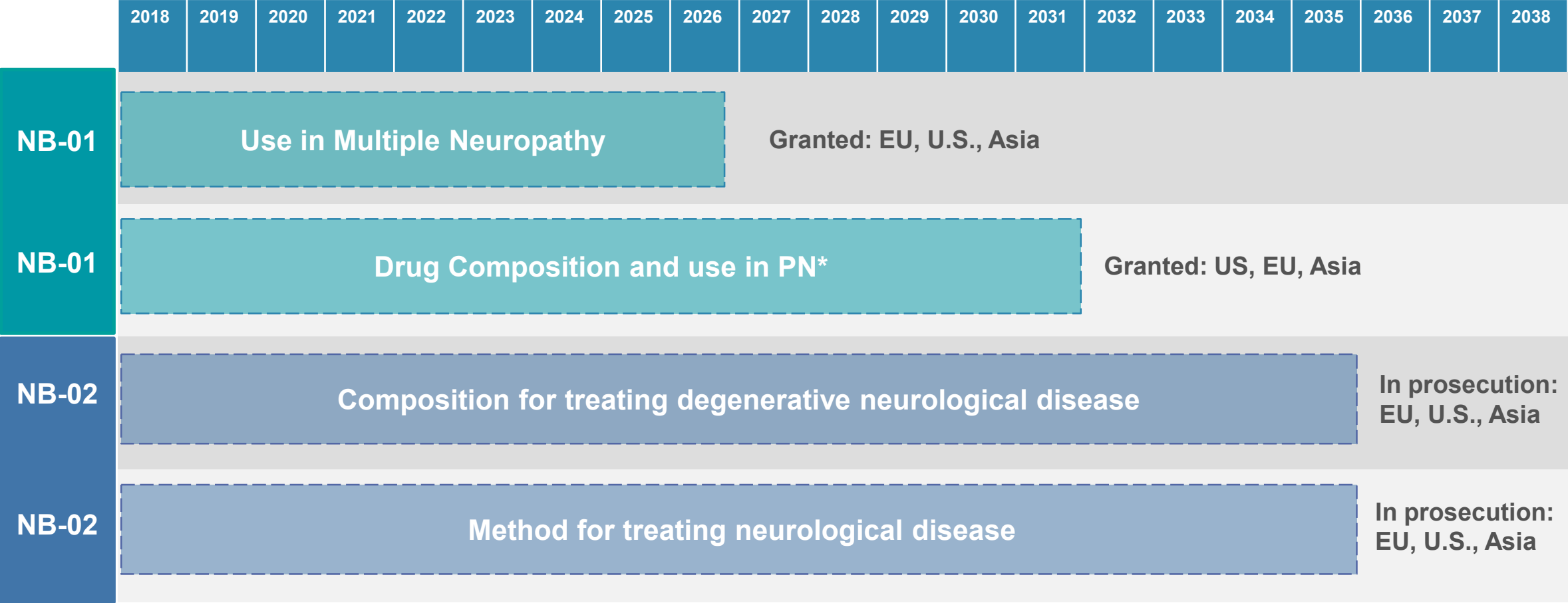
IND-enabling toxicology studies completed

26-week rat toxicity, 39-week dog toxicity, and other IND requirements done



PATENT PROTECTION FOR NB-01 AND NB-02

IP Protection for Indications and Long-Term Runway for Commercialization



*PN= Painful Neuropathy

INTELLECTUAL PROPERTY PORTFOLIO & FUTURE EXPANSION PLANS

NB-01

Drug Mixture
Composition

Peripheral
Neuropathy

- Granted patents in US, EU, and Asia on use of plant species in **treating multiple neuropathy** – Expires 2026
- Granted patents in US, EU and Asia, for **composition and use** in peripheral neuropathy – Expires 2031

NB-02

Drug Mixture
Composition

Neurodegenerative
disease

- Patents in prosecution for US, EU, and Asia on **composition comprising a combination of plant species** – estimated to expire 2035
- Patents in prosecution in US, EU, and Asia on **method for treating neurological disease** including Alzheimer's – Estimated to expire 2035

Ongoing Efforts to Extend Patent Life

Applications ongoing for:

1. **Marker assays**
2. **Markers linked to drug activity**

In Addition:

- Developing IP position on specific compounds within the drug mixtures linked to functional pathways responsible for therapeutic effect
- Patents being prosecuted for other indications



GEMCABENE

Targeting Cardiometabolic disease



GEMCABENE: NEAR-TERM CATALYST MAY PROVIDE FINANCIAL UPSIDE

- **Gemcabene**: a Phase 2b asset acquired in the reverse merger
 - Provides **potential financial upside** (subject to contingent rights[CVR] payments to pre-merger Gemphire stockholders)
 - PPAR (peroxisome proliferation activated receptor) agonist in development by Gemphire for the treatment of dyslipidemia
- FDA requires the completion of **two-year rat and mouse carcinogenicity** trials before conducting clinical trials of longer than six months.
- Submission of **request to lift partial clinical hold for gemcabene to the FDA is expected to occur in H1 2020**

We have taken the following actions in response to the clinical hold:

- Submitted a **2-year rodent carcinogenicity study** in 2018
- **Completed additional in-vitro PPAR- α transactivation study** in dog and monkey, per FDA request
- **Completed** a 13-week PPAR- α **knockout mouse study**, requested by FDA



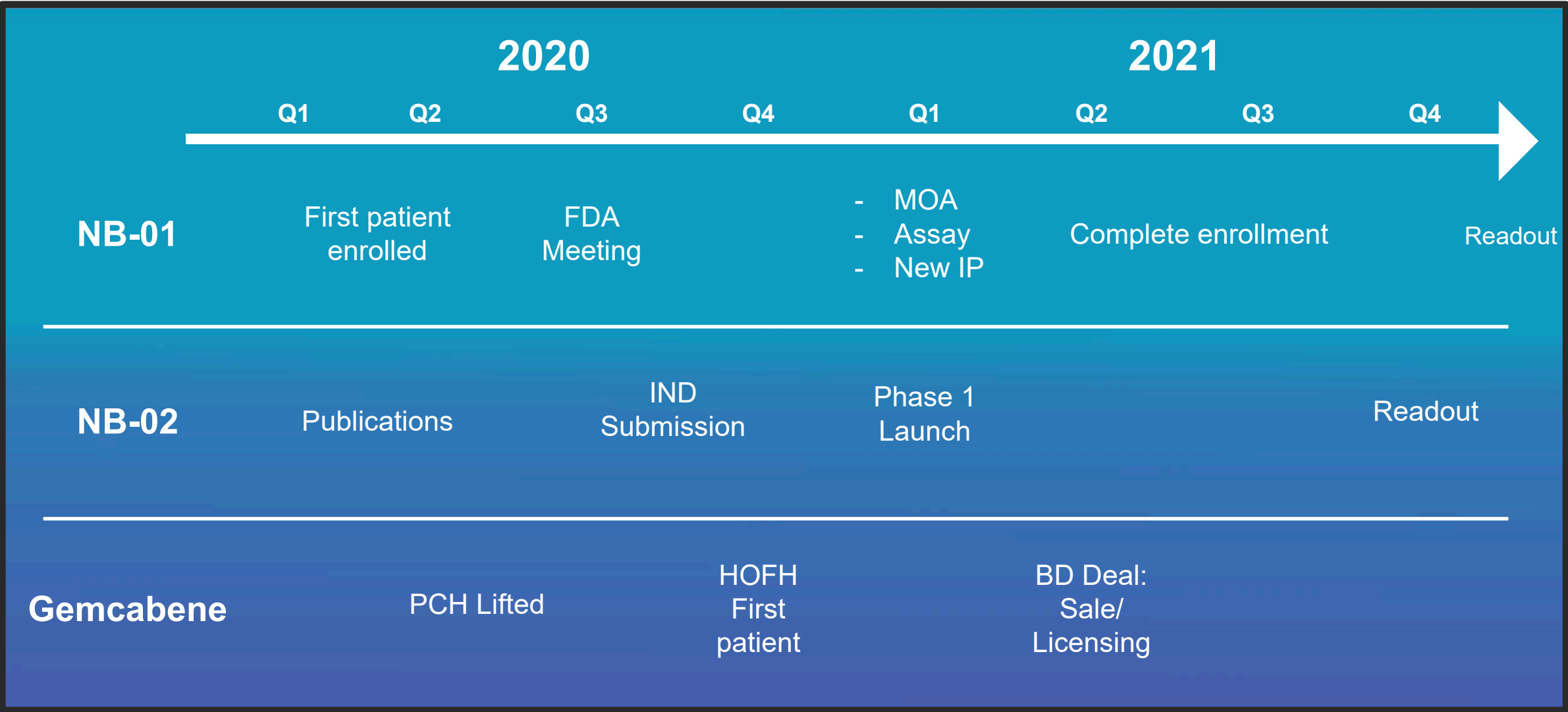
GEMCABENE: PHASE 2B ASSET WITH SIGNED PARTNERSHIP

- 25 completed Phase 1 and Phase 2 studies and **> 1,110 subjects treated with gemcabene** with multiple cardiometabolic indications studied, including Severe Hypertriglyceridemia ASCVD, Hypercholesterolemia, and Familial Partial Lipodystrophy, with promising results
- Gemphire signed an **out-licensing partnership with Beijing SL Pharmaceutical Co. Ltd.** to advance gemcabene, into the **Chinese market**
 - Provides **back end milestone and royalty payments** to NeuroBo if certain development and commercialization milestones are met
- **Pre-merger Gemphire stockholders received contingent value rights (CVRs)** entitling them to certain cash payments in the event the gemcabene assets are sold or licensed during the 10-year period following the closing of the merger or pursuant to the license agreement with Beijing SL





PIPELINE AND POTENTIAL MILESTONES WITH ADDITIONAL ASSETS



NEUROBO CAPITALIZATION TABLE

NASDAQ GLOBAL MARKET	
Symbol	NRBO
Market Cap ¹	\$140M
Price Per Share ¹	\$9.00
Shares Outstanding ²	15.6M
Combined Cash at 6/30/19	\$28.2M

1. 01/08/2020

2. Fully diluted shares outstanding = 16.6M as of 12/30/19





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