Novel Treatments for Neurodegenerative and Cardiometabolic Conditions

Multi-modal, disease-modifying therapies

Company Presentation
April, 2020
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COMPANY OVERVIEW AND REPOSITIONING OF NB-01

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

Repositioning Lead Program In Neuropathic Pain

**NB-01 – Pain Therapeutic Pivoting from Ph3 Trial to Nutraceutical Approval Pathway**
- Compelling Phase 2 data showing efficacy and safety for Painful Diabetic Neuropathy (PDN)
- Postponed Phase 3 study targeting PDN; In Q1 2020
- Preclinical showed NB-01 has multimodal mechanism of action to treat pain
- Combination of two natural products
- 18-24 months to commercialization; manufacturing in place
- Large and growing nutraceutical market of 15-20 million people in the U.S.

Two Programs Addressing Large Unmet Needs

**NB-02 - Targeting Alzheimer’s Disease (AD) and other dementias**
- IND Ready; Solid preclinical data

**Gemcabene: Targeting Dyslipidemias including orphan indications:**
- 25 Phase 1 and Phase 2 trials completed
- Awaiting FDA decision in Q2 to advance to Phase 3
- Asian partnership signed with Beijing SL to share cost of Phase 3 trial

Experienced Team with Capital Efficient Strategy

- Experienced executive team in drug development, natural products, strategy
- Reverse merger completed with Gemphire Therapeutics (Nasdaq: GEMP) on December 30, 2019; new NASDAQ listing (NRBO)

*Global Data*
PROVEN LEADERSHIP TEAM

Richard J. Kang, PhD
President & CEO
- Founder of JK BioPharma Solutions and senior management at companies including NeoImmuneTech 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 (Ervacycline)
- 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 Neuropathy
- 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 Bacskai, 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
<table>
<thead>
<tr>
<th>Disease Indication</th>
<th>Stage of Development</th>
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<tr>
<td></td>
<td>Discovery</td>
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<td><strong>NB-01</strong>&lt;br&gt;Painful Diabetic Neuropathy (PDN):</td>
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<tr>
<td><strong>NB-02 (IND-ready)</strong>&lt;br&gt;Alzheimer’s Disease</td>
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<td><strong>Gemcabene</strong>&lt;br&gt;HoFH</td>
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HoFH = Homozygous Familial Hypercholesterolemia  
SHTG = Severe Hypertriglyceridemia
NB-01
Targeting neuropathic pain
First indication: PDN
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
• 50% to 70% of patients still experience pain after typical first line therapy
  • Pain reduced only 20% more by typical second line therapy
• 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)
EXPLORING ADDITIONAL PATHWAYS
COVID-19 SHUTTERS GLOBAL CLINICAL TRIALS

• Nutraceutical pathway is a rapidly growing market for chronic pain
  • Patients are looking for alternatives to opioids, due to fear of addiction
  • Patients struggle with side effects from Neurontin and Lyrica as new boxed warnings for respiratory depression emerged in Dec. 2019

• Alternative pathway allows NB-01 to move forward in development while many other pharma companies can not proceed with clinical trials due to COVID-19

• Nutraceutical pathway reduces time and cost to market: Saves four years and over $100M in developmental R&D costs
  • Allows NB-01 to be cost competitive with CBD and generic Rx’s in a much larger chronic pain market

• Can compete in the fastest growing segment of the chronic pain market – CBD
  • NB-01 is non-opioid, non-psychotropic, natural product
  • Consistent and stable pharmaceutical grade CMC manufacturing process
EXPLORING ORPHAN INDICATIONS
PATIENTS WITH CRITICAL UNMET NEED IN CHRONIC PAIN

• Strong evidence of safety and efficacy observed in reducing chronic pain in patients
  • Two positive Phase 2 trials in treating painful diabetic neuropathy
  • Significant reductions from baseline in pain scores (NRS)^ observed
  • Significant reduction in rescue pain medications observed in Phase 2 US trial

• Exploring the opportunity for a POC* in orphan disease patient populations
  • Patient populations that suffer chronic neuropathic pain due to underlying orphan disease sequela
  • Offers efficient and focused clinical development approach to patients with the highest unmet needs
  • Potential for accelerated regulatory pathway review
  • Reduces cost of CMC**, commercial scale and manufacturing

^ NUMERICAL RATING SCALE (NRS)
* PROOF OF CONCEPT (POC)
** CHEMISTRY, MANUFACTURING AND CONTROLS (CMC)
FDA WARNING ON GABAPENTINOIDS FOR SERIOUS BREATHING PROBLEMS

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
SIGNIFICANT REDUCTIONS IN RESCUE MEDICATION OBSERVED IN 12-WEEK TRIAL WITH NB-01

Table 11-20: Average Weekly Rescue Medications Use, ITT Population - US Phase II Study

mg/day are mean values
50% RESPONSE RATES - COMPARISON OF NB-01 TO APPROVED THERAPIES

Pregabalin

Duloxetine

NB-01

Vasc Health Risk Manag. 2007;3(6):833-44
Pritchett, 2007 Pain Med 2007;8:397-409
### TEAEs with a ≥2% Difference (Safety Population)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Incident on NB-01 N=96</th>
<th>Incident on Placebo N=32</th>
<th>Difference in Incident NB-01 from Placebo</th>
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<tbody>
<tr>
<td>Constipation</td>
<td>5.2%</td>
<td>0.0%</td>
<td>5.2%</td>
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<tr>
<td>Sinusitis</td>
<td>5.2%</td>
<td>0.0%</td>
<td>5.2%</td>
</tr>
<tr>
<td>Back pain</td>
<td>6.3%</td>
<td>3.1%</td>
<td>3.1%</td>
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<tr>
<td>Myalgia</td>
<td>3.1%</td>
<td>0.0%</td>
<td>3.1%</td>
</tr>
<tr>
<td>Pain in extremity</td>
<td>3.1%</td>
<td>0.0%</td>
<td>3.1%</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>5.2%</td>
<td>3.1%</td>
<td>2.1%</td>
</tr>
<tr>
<td>Musculoskeletal pain</td>
<td>2.1%</td>
<td>0.0%</td>
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<tr>
<td>Nasopharyngitis</td>
<td>2.1%</td>
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<td>Pneumonia</td>
<td>2.1%</td>
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</table>

**Duloxetine**
- Most common adverse reactions (≥5% and at least twice the incidence of placebo patients): nausea, dry mouth, somnolence, **constipation**, decreased appetite, and hyperhidrosis

**Pregabalin**
- Most common adverse reactions (greater than or equal to 5% and twice placebo) in adults are dizziness, somnolence, dry mouth, edema, **blurred vision**, weight gain, and thinking abnormal (primarily difficulty with concentration)

Source: DA9801-DN-001 (USA) Table 14.3.1.1A
DISTINCT MULTI-TARGET APPROACH: PRE-CLINICAL DATA

Anti-inflammatory

Nerve growth and repair

Reducing cell damage

Reduction IL-6 Expression in STZ model

NGF restored to normal endogenous levels in STZ model

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

Note: DA-9801 is now NB-01
* Data on file NeuroBo
EXPLORING OPPORTUNITIES BEYOND TRADITIONAL PDN TREATMENT PARADIGM

Confirmed painful diabetic neuropathy

First Line
- Tricyclic antidepressants
  - Amitriptyline
- Serotonin-norepinephrine reuptake inhibitors
  - Duloxetine (Cymbalta®)
  - Venlafaxine
- Voltage-gated calcium channel α2δ ligands
  - Pregabalin (Lyrica®)
  - Gabapentin

No Effect \(\Rightarrow\) Partial Effect

Second Line
- Try another first-line drug
- Or
- Try combination of first-line drugs

Third Line
- If all three classes and combination therapy fail

- Opioids

- 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

Source: Adapted from Callahan et al., 2012
Gallop poll: 14% of Adult Americans Say They Use CBD Products

40% of patients said they use it for pain
NB-02

Targeting Alzheimer’s disease & Other Dementias
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**

**Restores Disrupted Ca++ Homeostasis**

**Inhibits Tau Phosphorylation**

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

DA – NB-01
DPZ – Donepezil
LY – β-secretase inhibitor

Pagnier et al., 2018
Alzheimer Research & Therapy
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

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<td>2038</td>
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**NB-01**
- **Use in Multiple Neuropathy**
  - Granted: US, EU, Asia

**NB-01**
- **Drug Composition and use in PN***
  - Granted: US, EU, Asia

**NB-02**
- **Composition for treating degenerative neurological disease**
  - Granted: US, EU, Asia

**NB-02**
- **Method for treating neurological disease**
  - In Prosecution: US, EU, Asia

*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

- Granted patents in US, EU, and Asia on composition comprising a combination of plant species – Expires 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
## UPCOMING MILESTONES
DEVELOPMENT INTO 1H 2021

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<td><strong>1H 2020</strong></td>
<td><strong>Assess alternative Pathways:</strong></td>
<td><strong>Publications</strong></td>
<td><strong>Expected response on partial</strong></td>
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<td></td>
<td>• Nutraceutical</td>
<td>IP Development</td>
<td>clinical hold</td>
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<td>• Orphan CMC (assess)</td>
<td>CMC development</td>
<td>IP Development</td>
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<td>Exploring other indications for Orphan Drug</td>
<td>Maintain CMC – Clinical supply</td>
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<td><strong>Publications</strong></td>
<td><strong>Publications (cont.)</strong></td>
<td>If PCH is Positive:</td>
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<td><strong>CMC development (cont.)</strong></td>
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<td>• Evaluate strategic partners</td>
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### NASDAQ CAPITAL MARKET

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<tr>
<td><strong>Symbol</strong></td>
<td>NRBO</td>
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<tr>
<td><strong>Market Cap(^1)</strong></td>
<td>$281M</td>
</tr>
<tr>
<td><strong>Price Per Share(^1)</strong></td>
<td>$18.04</td>
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<tr>
<td><strong>Shares Outstanding(^2)</strong></td>
<td>15.6M</td>
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<tr>
<td><strong>Combined Cash at 12/31/19</strong></td>
<td>$13.9M</td>
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</table>

1. 04/06/2020
2. Fully diluted shares outstanding = 16.6M as of 12/31/19