BELLUS Health and NEOMED Institute Transaction

Licensing of BLU-5937 for Chronic Cough

February 28, 2017
Investment Thesis

BLU-5937: potential to be best-in-class drug addressing high unmet need
- Orally bioavailable small molecule
- Superior potency and P2X3 selectivity
- Potential for improved efficacy and safety profile
- Clear and efficient development path & value creation

P2X3: validated target in emerging drug class for chronic cough
- Merck acquired a P2X3 antagonist program in 2016 for US$500M based on positive Phase II data in chronic cough
- Potential multi billion dollar drug class in therapeutic indication lacking innovation

Right-sized transaction for BELLUS
- Attractive financial terms
- Leverages core competencies: clinical, BD, financing
- Experienced, motivated team to drive project to success

Fast follower with best-in-class potential for large market with high unmet medical need
### Chronic Cough

Cough lasting > 8 weeks, associated with:

- Pulmonary diseases (asthma, COPD, lung cancer, IPF)
- Extra-pulmonary disorders (post-nasal drip, gastro-oesophageal reflux)
- Use of certain drugs (ACE inhibitors)
- No identifiable cause (unexplained chronic cough)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Implications</th>
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<td>Time and resource intensive for healthcare system</td>
<td>Responsible for 30M physician visits per year in U.S.</td>
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<td>38% of pulmonologist outpatient practice</td>
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<td>Unexplained and refractory chronic cough require time and resource intensive differential diagnosis</td>
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Major Impact on Patients

Chronic cough has significant impact on patient quality of life

Social complications
- Embarrassment of coughing in public
- Interference with lifestyle, work & leisure
- Difficulty speaking
- Social exclusion

Physical complications
- Exhaustion
- Sleep deprivation
- Retching/vomiting
- Incontinence
- Headache
- Hoarse voice
- Chest pain
- Rib fracture

Psychosocial complications
- Distress
- Anger
- Anxiety
- Depression
## Few Treatment Options

<table>
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<tr>
<th>Opioids</th>
<th>Gabapentin/Pregabalin</th>
<th>OTC Products</th>
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<td>Some efficacy but cause sedation/confusion</td>
<td>Centrally acting</td>
<td>Very limited efficacy</td>
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<tr>
<td>Constipation and nausea</td>
<td>Some efficacy demonstrated in small studies</td>
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<td>Potential for addiction</td>
<td>High incidence of adverse effects</td>
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No novel approach approved to address chronic cough in 40 years
Pathophysiology: Hypersensitivity of Cough Reflex

Coughing trigger (ex. asthma attack)

Cellular damage causes ATP release in respiratory tract

ATP activates P2X3 receptors on airway sensory neurons

Cell injury

Airway hyper-excitability

Chronic Cough

Drug targeting P2X3 has strong mechanistic rationale for reducing cough frequency
Weakly selective P2X3 antagonist use in chronic cough patients results in:

50 to 75% reduction in cough frequency

50 to 100% of patients experience taste disturbance

Problematic taste side effect likely due to lack of high selectivity for P2X3

Opportunity for highly selective P2X3 antagonist with better efficacy/safety profile ratio to become class leader


P2X3 Family Involved in Taste Perception

Taste stimuli

ATP release from taste buds

ATP activates P2X3 and P2X2 receptors on taste sensory neurons

Taste perception

Drug with high selectivity for P2X3 could limit or eliminate taste alteration side effect without compromising effect on cough

Strong drug candidate profile with potential to be best in P2X3 class.

Orally bioavailable small molecule

High Potency (low nM) and Selectivity for P2X3

Zero safety findings of concern to-date

Broad and comprehensive IP to 2034

Kg scale CMC
Preclinical Efficacy: Cough Response

Oral administration of BLU-5937 dose-dependently reduced the frequency of cough in a guinea pig model.

Treatments (control, BLU-5937) were administered orally (p.o.) two hours prior to tussive agent exposure: citric acid (0.1 M, aerosol) and histamine (0.6 mM, aerosol); n=6 animals (guinea pig) per group *p<0.05
**Competitive Landscape**

**TRP modulators**
- Novel target, TRPM8, is in the exploratory stage with limited mechanistic understanding

**NK1 antagonists**
- Repurposed class initially developed for depression
- Also target sensory nerve signaling
- Limited clinical validation in chronic cough

**P2X3 antagonists**
- Inhibit respiratory tract sensory pathway signals
- Most promising and competitive novel class of anti-tussive

Acquired by Merck in 2016 (US$500M upfront, US$750M in milestones) following positive Phase II data
10-40% patients with refractory / unexplained chronic cough

10% of US adult population has chronic cough

Estimated addressable patients in major pharma markets: 6.3M

Major pharma markets include the U.S., Europe top five countries and Japan


Zanasi et al., 2014. Chronic and unexplained cough. (Published online) Vol 4, No 3 pp. 159-164
## Key Development Milestones

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<th>2017</th>
<th>2018</th>
<th>2019/2020</th>
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<td>IND-enabling studies</td>
<td>Phase I: assess dose and taste effect</td>
<td>Phase II: demonstrate antitussive effect</td>
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<tr>
<td>Complete IND preclinical study package</td>
<td>Assess safety, tolerability, PK, effect on taste in healthy subjects</td>
<td>Assess safety, PK and antitussive effects in patients suffering from chronic refractory cough</td>
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<td>Single ascending dose and multiple ascending dose studies</td>
<td>Dose response study with crossover design</td>
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Value creating milestones throughout development path
Key Transaction Terms

Scope: exclusive worldwide license for all indications

Upfront Fee: $1.7M cash; $1.5M equity

Royalty Rate: Low single digit tiered

Revenue Sharing: Very low double digit revenue sharing expected

Milestone Payments: None

Significant upside potential for BELLUS investors