



Bellus
HEALTH

BELLUS Health and NEOMED Institute Transaction

Licensing of BLU-5937 for Chronic Cough

February 28, 2017

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

Characteristics

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)

Implications

Time and resource intensive for healthcare system

- Responsible for 30M physician visits per year in U.S.
- 38% of pulmonologist outpatient practice
- Unexplained and refractory chronic cough require time and resource intensive differential diagnosis

Major Impact on Patients

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

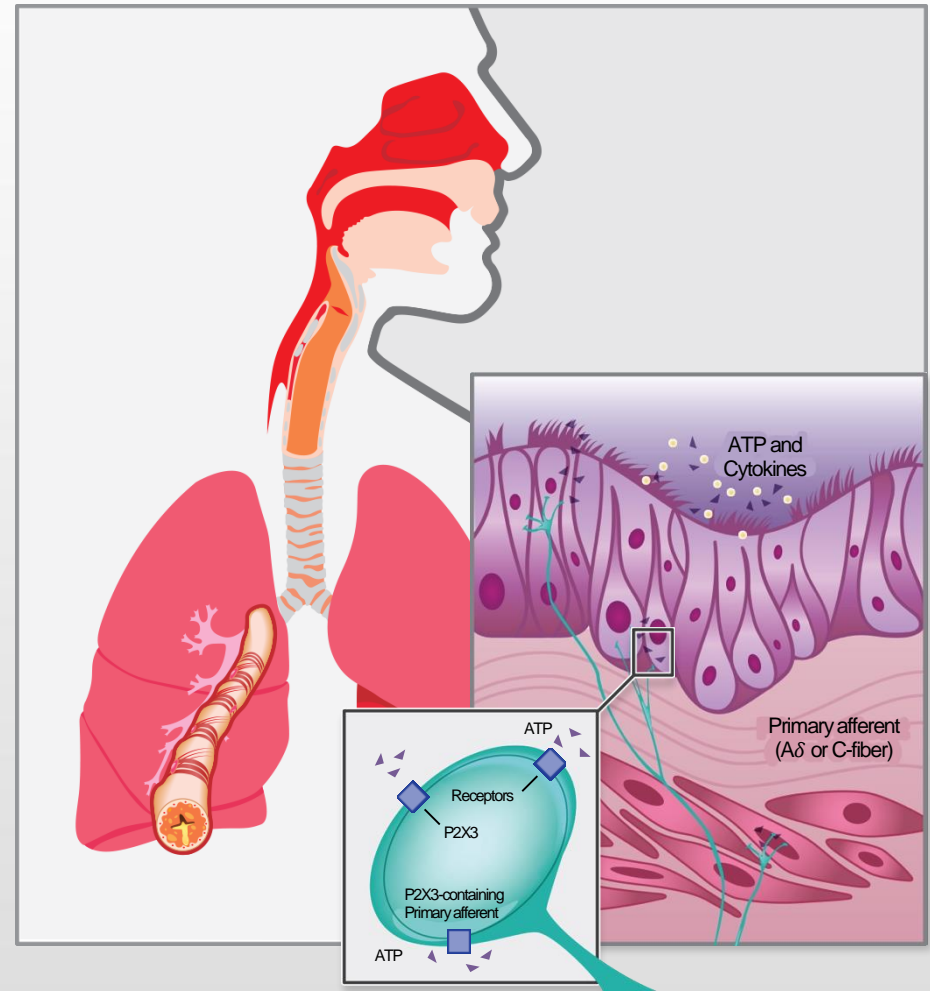
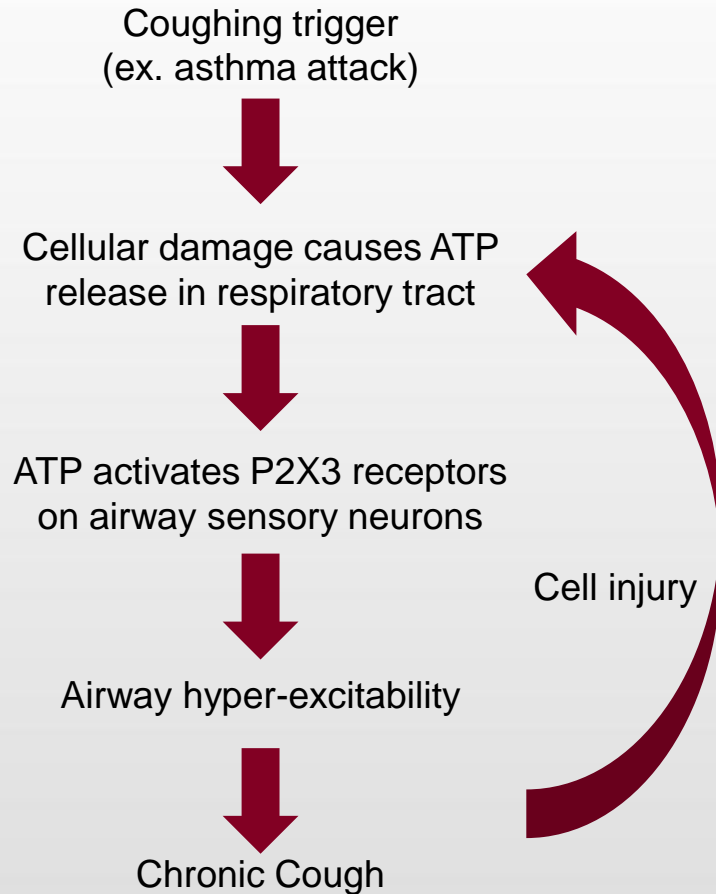
Chronic cough has significant impact on patient quality of life

Few Treatment Options

Opioids	Gabapentin/Pregabalin	OTC Products
Some efficacy but cause sedation/confusion Constipation and nausea Potential for addiction	Centrally acting Some efficacy demonstrated in small studies High incidence of adverse effects	Very limited efficacy

No novel approach approved to address chronic cough in 40 years

Pathophysiology: Hypersensitivity of Cough Reflex



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

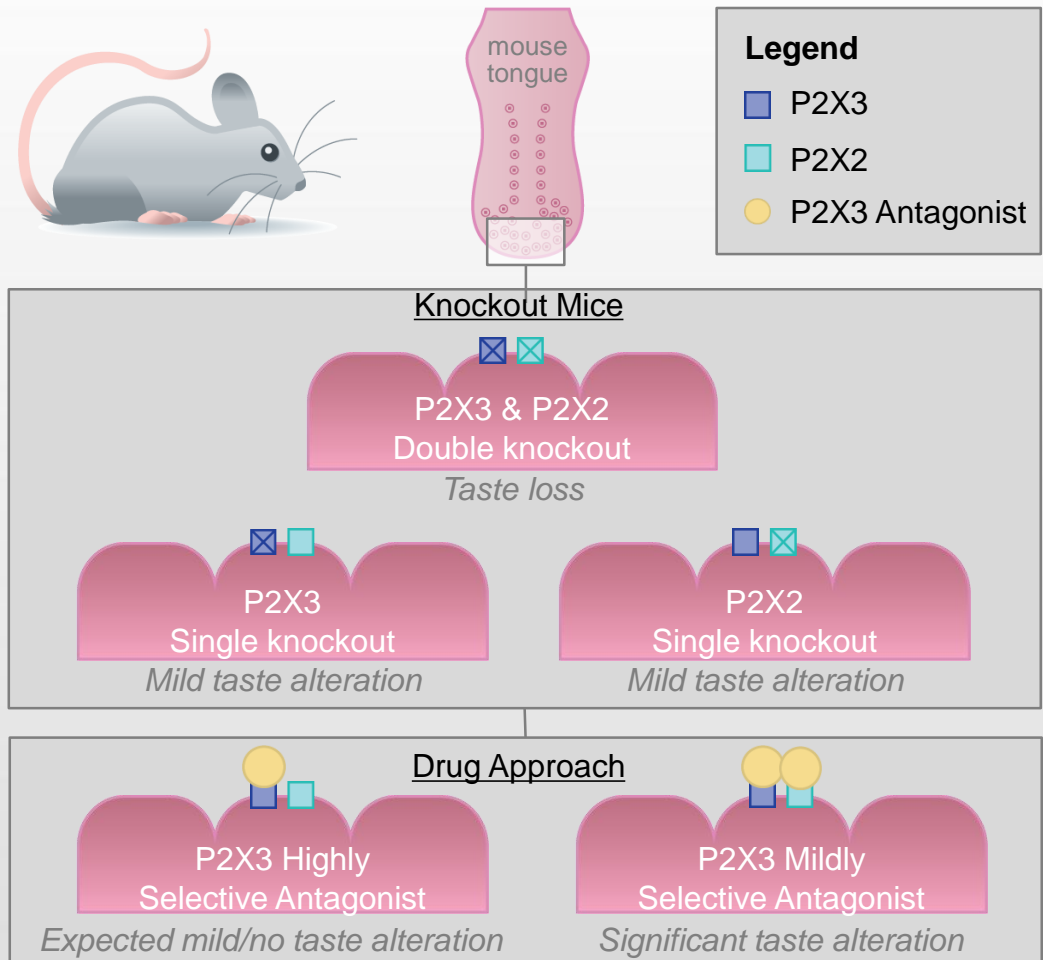
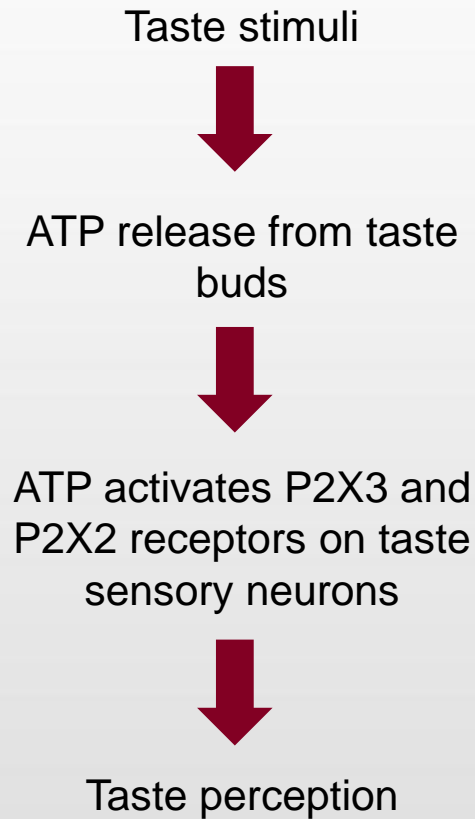
50 to 100%
of patients experience taste disturbance

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

Abdulqawi et al., 2016. P2X3 receptor antagonist (AF-219) in refractory chronic cough: a randomised, double-blind, placebo-controlled phase 2 study. *Lancet*. Vol 385, No 9974 pp. 1198-1205.
Kitt et al., 2016. A Phase 2 Dose-Escalation Study with AF-219, a P2X3 Antagonist for the Treatment of Chronic Cough. American Thoracic Society 2016 International Conference - San Francisco.

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

P2X3 Family Involved in Taste Perception



Kinnamon et al., 2013. A Taste for ATP: neurotransmission in taste buds. *Frontiers in Cellular Neuroscience*. Vol 7, Article 264 pp. 1-7.

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

Orally bioavailable
**small
molecule**

High

Potency (low nM)
and Selectivity for
P2X3

Zero

safety findings of
concern to-date

Broad and
comprehensive IP to

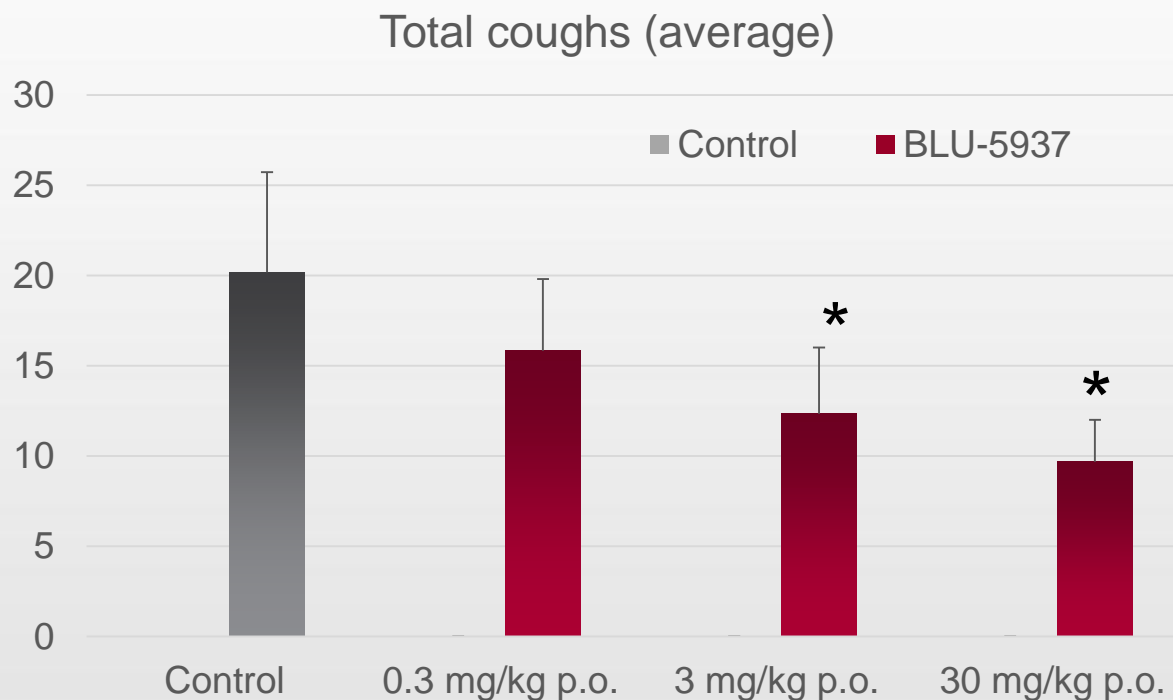
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Kg

scale CMC

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

Preclinical Efficacy: Cough Response

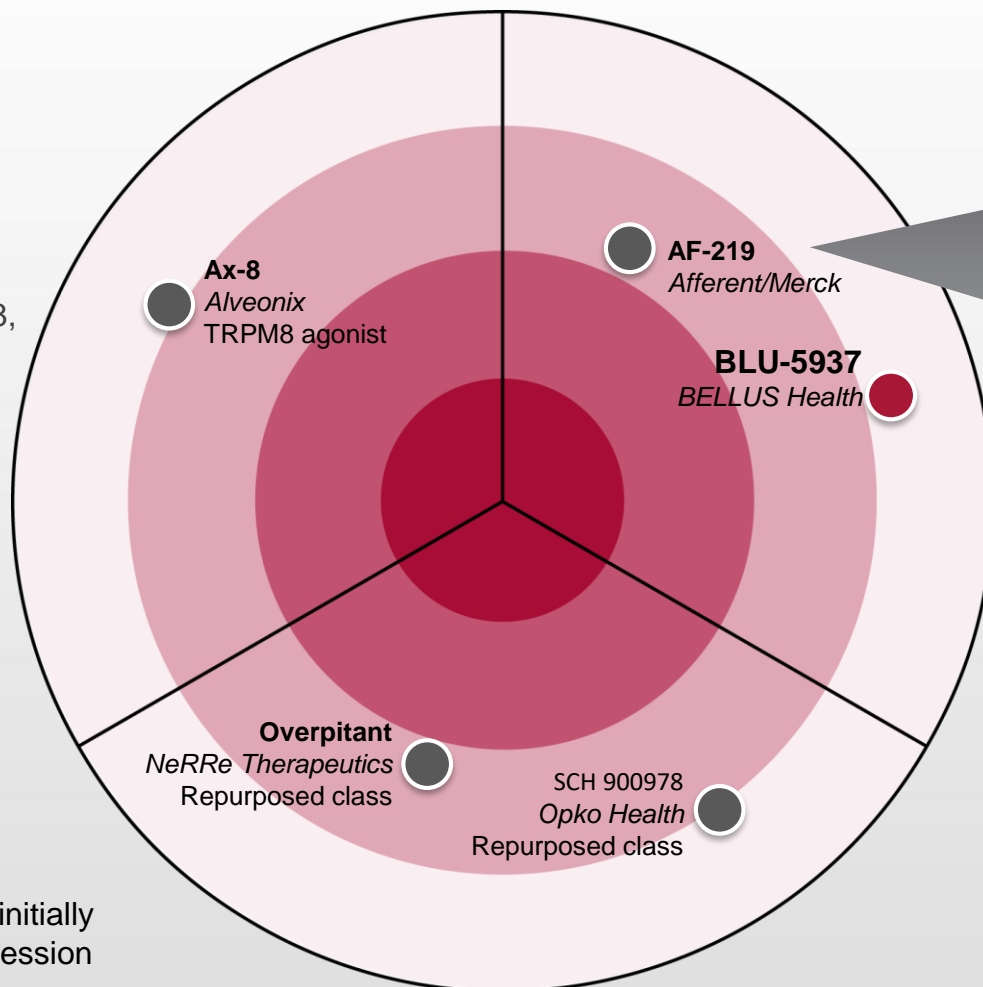


Treatments (control, BLU-5937) were administered orally (p.o.) two hours prior to tussive agent exposure: citric acid (0.1 M, aerosol) and histamine (0.6 mM, aerosol); n=6 animals (guinea pig) per group *p<0.05

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

TRP modulators

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



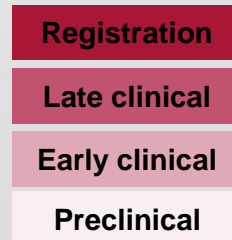
Acquired by Merck in 2016 (US\$500M upfront, US\$750M in milestones) following positive Phase II data

NK1 antagonists

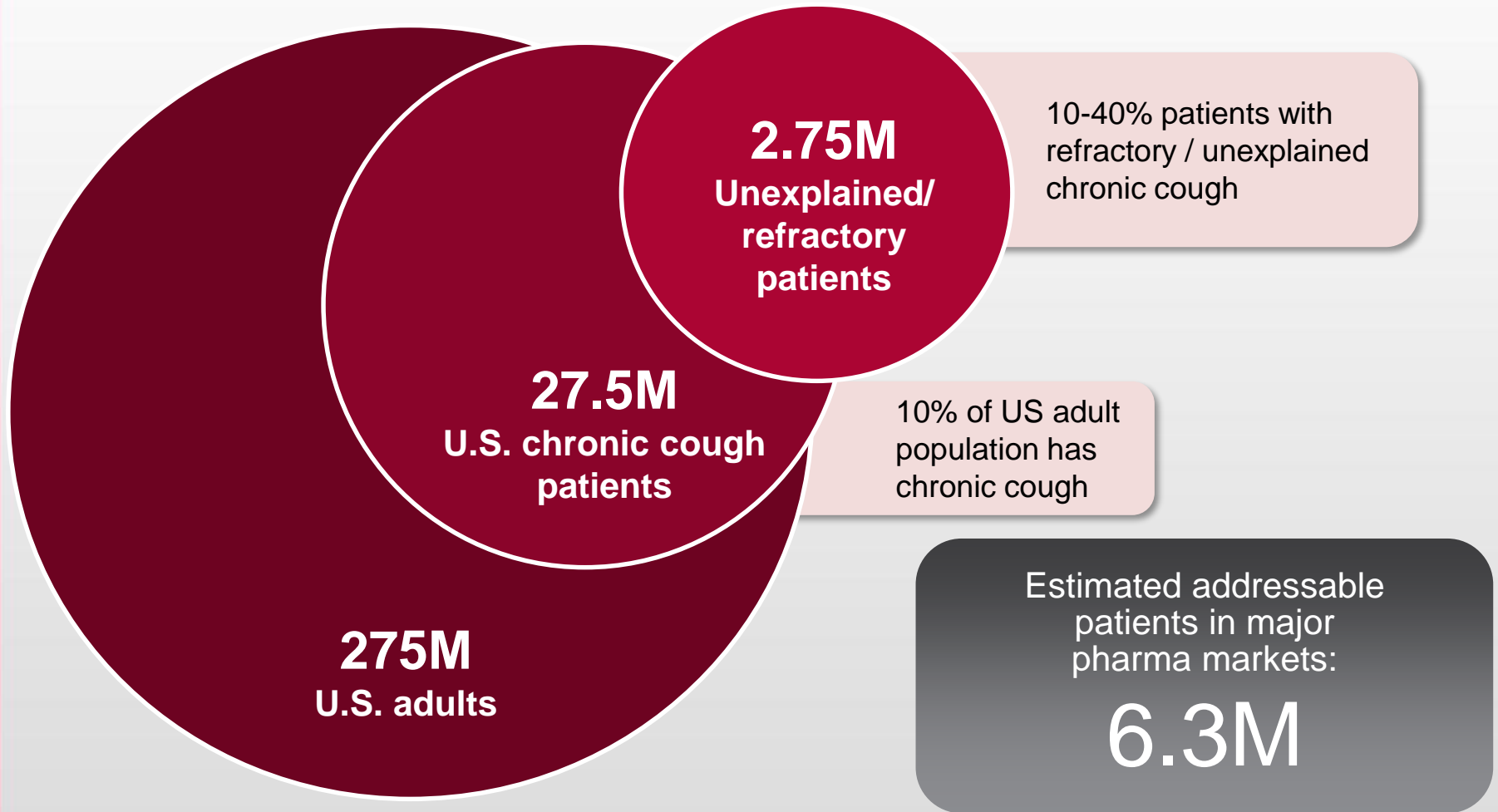
- Repurposed class initially developed for depression
- Also target sensory nerve signaling
- Limited clinical validation in chronic cough

P2X3 antagonists

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



Large Addressable Market



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

Song et al., 2015. The global epidemiology of chronic cough in adults: a systematic review and meta-analysis. *Eur Respir J.* Vol 55 pp. 1479-1481

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

Key Development Milestones

2017	2018	2019/2020
IND-enabling studies	Phase I: assess dose and taste effect	Phase II: demonstrate antitussive effect
Complete IND preclinical study package	Assess safety, tolerability, PK, effect on taste in healthy subjects Single ascending dose and multiple ascending dose studies	Assess safety, PK and antitussive effects in patients suffering from chronic refractory cough Dose response study with crossover design

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