



Bloom Burton Healthcare Conference

TSX: BLU

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Roberto Bellini

President and Chief Executive Officer

Twitter: @rbellini

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Lead program

P2X3 antagonist

BLU-5937

for chronic cough

Large population with significant need

Targeted by big pharma – Merck/Bayer

Phase 1 confirms best in class potential

Clinically validated target reduces clinical risk

Phase 2 starting mid 2019

Experienced

management with track record of execution

Important US institutional ownership with

~2

years cash runway

Potential to build

P2X3 Platform

Generating value by advancing drug candidates through clinical studies

Team



Management



Roberto Bellini
President &
Chief Executive Officer



Dr. Denis Garceau
Senior Vice President,
Drug Development



François Desjardins
Vice President,
Finance



Tony Matzouranis
Vice President,
Business Development

Board of Directors



PICCHIO
INTERNATIONAL

Dr. Francesco Bellini
(Chair)



Franklin Berger



Pierre Larochelle



Dr. Clarissa Desjardins



Dr. Youssef Bennani



Chau Q. Khuong



Joseph Rus



Roberto Bellini

Management with a track record of execution

Problem: Refractory Chronic Cough

Cough lasting
≥8 weeks,
0 therapies that are
safe **and** effective

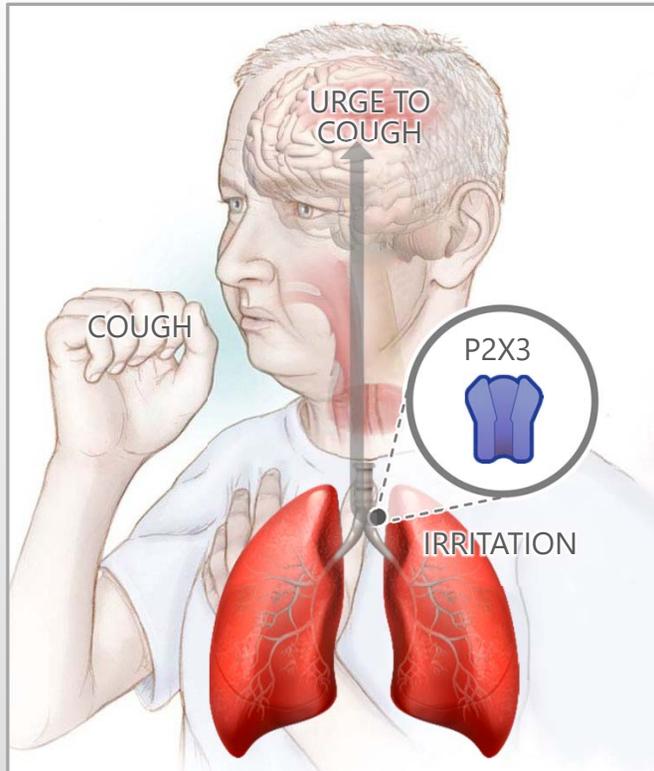
Major
impact on quality
of life

"I see patients that have been coughing 2 months to 30 years. Within that group, there is a good portion where I am the 8th or 10th doctor."

– Chronic Cough KOL

2.6M
patients in U.S. with longstanding
refractory chronic cough

Multi \$B
market potential



P2X3 Receptor in Refractory Chronic Cough

- P2X3 is an ATP gated ion channel in the peripheral nervous system
- Key sensory receptor in feeling upper airway irritation and triggering cough reflex
- Targeting P2X3 with an antagonist is a validated approach to treating chronic cough in animals and humans

P2X3 is a rational target for treating refractory chronic cough that has been validated in animal and human studies

Treatment in Development is Suboptimal



Effective

Reduces awake
cough frequency by
86%



Mechanism:
P2X3
antagonist

Major Side Effect

80%
of patients have taste
alteration or taste loss

Merck & Co., Inc. (2017). Merck Announces Presentation of Phase 2 Results for MK-7264, an Investigational, P2X3 Receptor Antagonist, Being Evaluated for the Treatment of Chronic Cough. [Press Release]. Retrieved from <http://www.mrknewsroom.com/news-release/research-and-development-news/merck-announces-presentation-phase-2-results-mk-7264-inve>

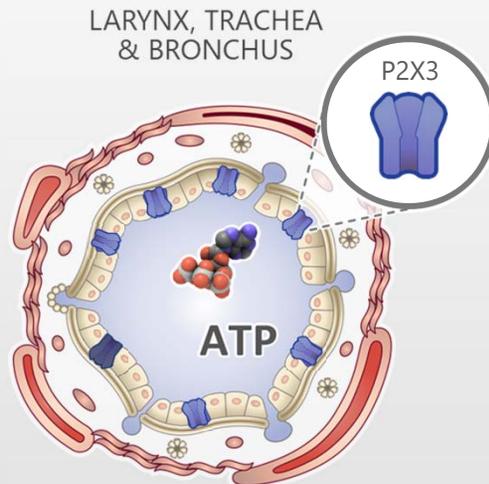
Acquired in 2016 for \$1.25B (\$500M upfront) based on phase 2 data and currently in two Phase 3 studies

MK-7264 Effect on Taste Likely Caused by Inhibition of P2X3 and P2X2/3

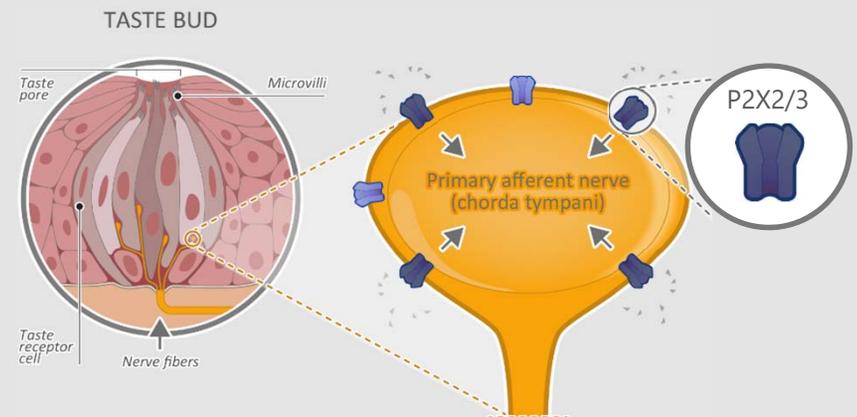
P2X3 and P2X2/3 are ATP-gated ion channels that transmit sensory signals:



P2X3 homotrimers have primary role in **cough reflex**



P2X2/3 heterotrimers have major role in **taste**



Project hypothesis: Opportunity for highly selective P2X3 antagonist to reduce cough, maintain taste (no P2X2/3 inhibition)

Highly potent

P2X3 antagonist

Low nM IC₅₀



Equivalent

reduction in
cough frequency¹

¹vs. MK-7264 in animal studies

Highly selective

P2X3 antagonist

~ 1500X selectivity vs P2X2/3



Little/No

impact on taste²

²Bellus Phase 1 data



BLU-5937 has key characteristics to test hypothesis and already validated in animal models

BLU-5937 Taste Profile Differentiated

Incidence and Severity of Taste Effect AEs at Estimated Comparative Therapeutic Doses

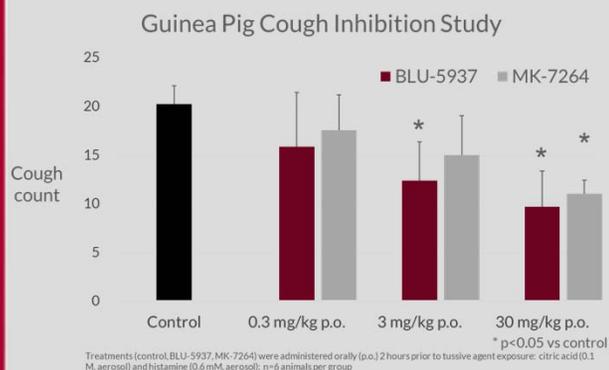
	BLU-5937 (50-100 mg) (n=24)	MK-7264¹ (50 mg) (n=57)
Study	NCT03638180	NCT02612610
Dose(s)	50 and 100 mg single dose and 7 day BID cohorts	50mg BID arm for 12 weeks
Subjects	Healthy volunteers	Refractory chronic cough
Taste alteration	<5%	48%
Partial taste loss	0%	24%
Complete taste loss	0%	20%
All taste adverse events	<5%	81%

At estimated therapeutic doses, BLU-5937 has significantly improved taste effect profile versus gefapixant

¹Merck & Co Presentation of gefapixant Phase 2b data at American Thoracic Society 2017

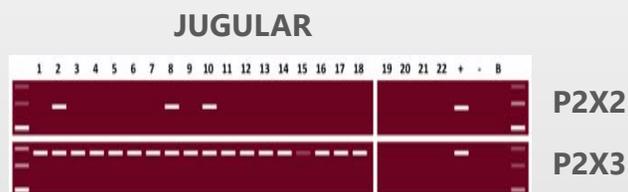
Taste effect profile significantly improved with BLU-5937 vs gefapixant

Validated Efficacy Target Reduces Clinical Risk

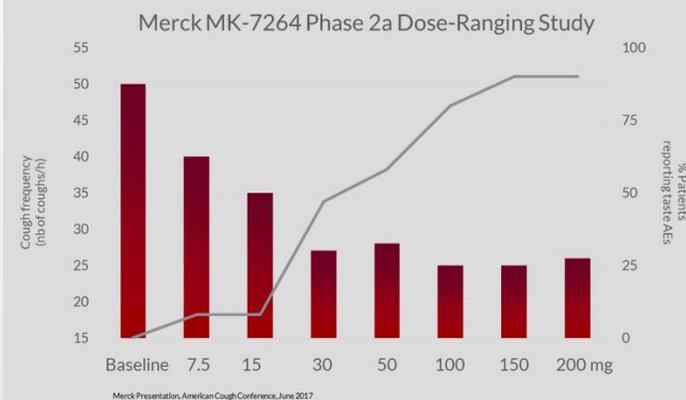


BLU-5937 Has Comparable Efficacy to MK-7264 in Animal Model

P2X3 is the Principal Receptor in the Upper Airway



Kwong et al 2008: Single-cell RT-PCR analysis of 22 lung specific guinea pig jugular neurons



Inhibition of P2X3 Linked to Efficacy and Inhibition of P2X2/3 Linked to Taste Effect in MK-7264 Phase 2 Study

Mechanistic, anatomy, animal and clinical data supportive of BLU-5937 having similar efficacy to MK-7264; Phase 2 starting in mid 2019

P2X3 Antagonist Competitive Landscape



Merck MK-7264

Bayer BAY 1817080

Shionogi S-600918

BELLUS BLU-5937

	Merck	Bayer	Shionogi	BELLUS
Phase	3	3	2	1
Dosing	15 mg B.I.D.	45 mg B.I.D.	B.I.D.	Q.D.
Selectivity for P2X3 (vs. P2X2/3)	2 - 7 x	2 - 7 x	25 - 125 x *	~ 1500 x
Anti-tussive effect [†]	Low	High	High	High
Effect on taste [†]	Low	High	Moderate/Low	Moderate/Low

Best in class selectivity for P2X3 supports potential best in class profile ←

* Bayer selectivity range of 419 P2X3 antagonists described in Bayer US patent 10,183,937 for a total

** Shionogi selectivity value presented in Tobinaga et al., 2017 for a representative, single, optimized P2X3 antagonist generated by Shionogi (may not be S-600918)

† Effect on taste and anti tussive effect are company estimates based on animal data, clinical data, dose, human P2X3 potency and human P2X3 vs P2X2/3 selectivity

BLU-5937 is potential best-in-class profile in large, big pharma validated, cough market

Key Objectives

Assess Safety

Assess Tolerability
including Taste
Effect

Assess
Pharmacokinetic
Profile and Select
Doses for Phase 2

Single Ascending Dose

N = 60 healthy adult subjects
6 cohorts of 10 subjects (8 active: 2 placebo) administered single dose
Single doses of 50mg to 1200mg
Food interaction tested in 1 cohort (200mg)

N = 30 healthy adult subjects
3 cohorts of 10 subjects (8 active: 2 placebo) administered multiple dose
Doses of 100, 200 and 400mg BID for 7 days

Multiple Ascending Dose

Phase 1 designed to assess safety, tolerability (including taste effect) and pharmacokinetic profile

Phase 1 Pharmacokinetic Profile and Dosing

Pharmacokinetic Profile

- Rapidly absorbed (Tmax ~1h)
- Systemic exposure increases dose proportionally up to 800 mg
- Plasma half-life of 4 to 9 hours
- No significant food effect
- No significant drug systemic accumulation

Excellent PK Profile

Dosing

Optimal projected
therapeutic dose of:
50-100mg
twice daily

Based on achieving targeted receptor inhibition & efficacy seen in preclinical studies and on achieving comparative drug blood levels of clinically validated comparator

Excellent PK profile supporting estimated optimal efficacy dose of 50mg - 100mg twice daily

Phase 1 - Safe and Well Tolerated

Safe and Well Tolerated

- Incidence of adverse events on BLU-5937 (44%) similar to placebo (50%)
- No serious adverse event (SAE) reported
- No subject withdrew prematurely due to adverse event
- No clinically significant effect on vital signs and ECG
- No clinically significant trends of changes in laboratory tests

Side Effects

- At expected therapeutic doses (50-100mg; n= 24), no side effects of concern:
 - Taste alteration <5%
 - Headache <10%
 - Heartburn <5%

Safe and well tolerated particularly at projected optimal therapeutic doses

Minimal Taste Effect at Therapeutic Doses

Incidence of Taste AEs (All SAD and MAD Cohorts)

	50mg (n=8)	100mg (n=16)	200mg (n=16)	400mg (n=16)	800mg (n=8)	1200 mg (n=8)
Taste alteration	0 (0%)	1 (6%)	0 (0%)	6 (38%)	5 (63%)	2 (25%)
Partial taste loss	0 (0%)	0 (0%)	0 (0%)	1 (6%)	1 (13%)	0 (0%)
Complete taste loss	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

- No complete taste loss at any dose
- One subject out of 24 (4%) reported taste alteration at the anticipated therapeutic doses (50-100 mg)
- No taste loss or taste alteration at 200 mg
- Two subjects reported mild, transient partial loss of taste
- All taste adverse events were transient and sporadic in nature; one rated moderate, all others mild

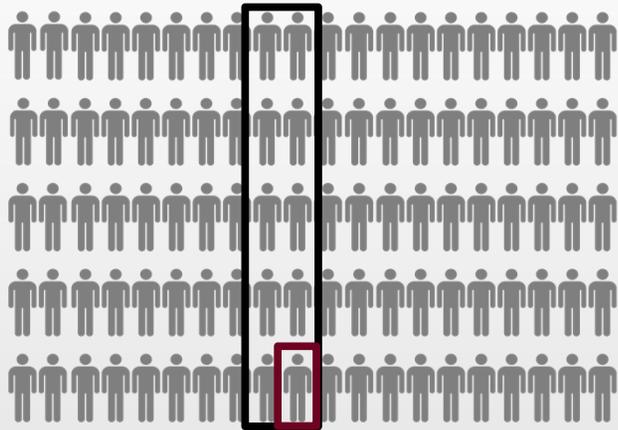
Low incidence of taste AEs particularly at optimal projected therapeutic doses (1/24 = <5%)

1 subject at 100mg BID had transient taste alteration (2 episodes on day 1 out of 7 days of dosing)

No to minimal taste effect at projected therapeutic doses; taste AEs at supra-therapeutic doses are generally mild and transient in nature

Market

263M U.S. adults



Large addressable patient population

10% or 26.3M
chronic cough patients

2.6M
Primary addressable patients
(idiopathic, treatment refractory > 1 yr)

Comparable products



Payer discussions and comparable product analysis support \$300-600 per month pricing

Report 2018 Bluestar BioAdvisors (formerly known as Torrey Insights)

BLU-5937: addressing potential multi billion dollar refractory chronic cough market

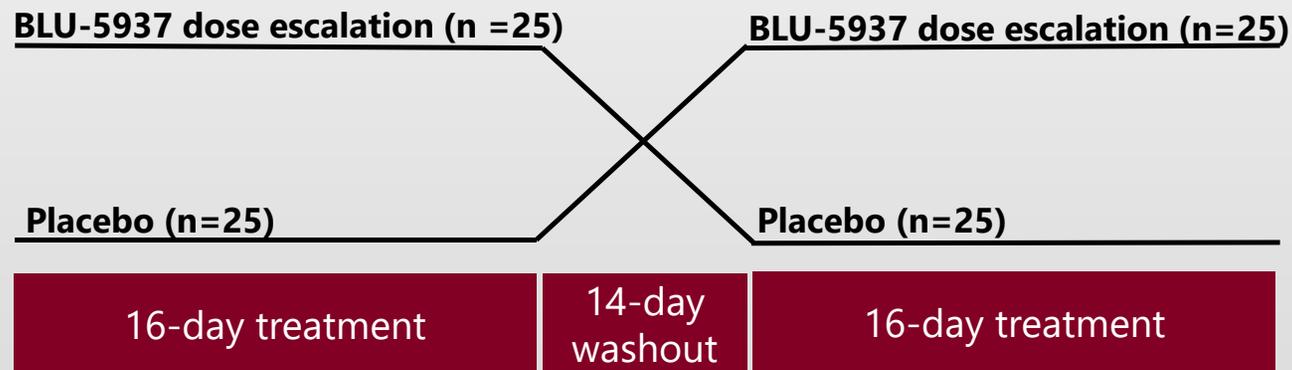
Key Development Milestones



Validated and efficient development plan

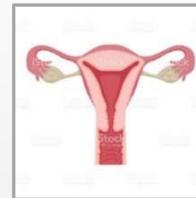
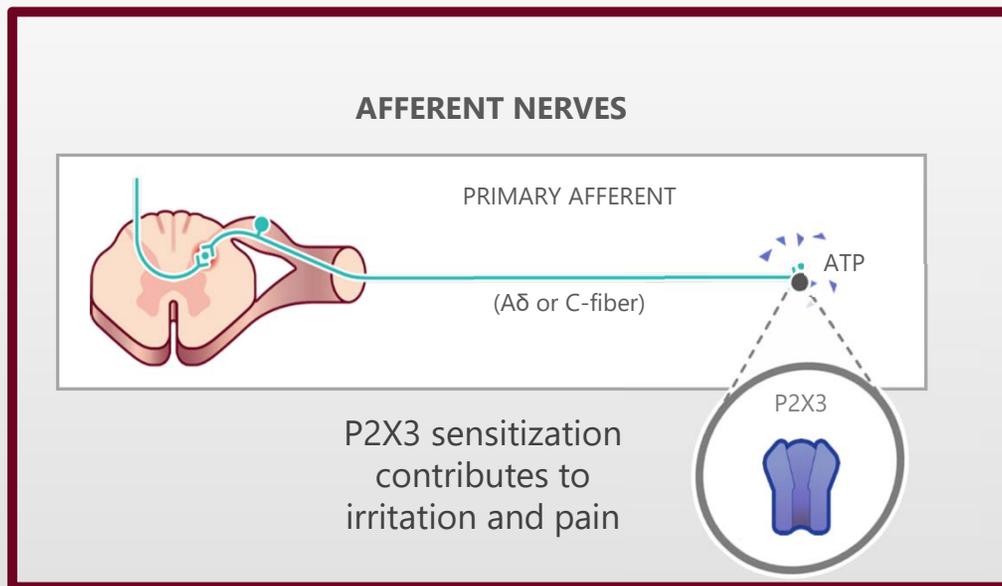
Phase 2 Study Design

- N≈50 unexplained/refractory chronic cough patients; >1 year coughing
- 12 sites in UK and US
- 4 dose levels with forced escalation at 4-day intervals (25/50/100/200mg twice daily)
- Primary endpoint: Reduction in awake cough frequency using cough recorder
- Safety and tolerability assessment, including taste effect



Phase 2 expected to start in mid 2019 with topline data in mid 2020

Potential for P2X3 Indication Expansion



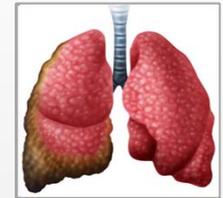
ENDOMETRIOSIS PAIN

Phase 2 study started by Merck



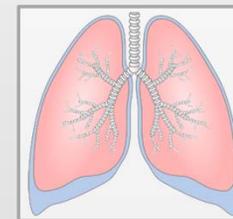
OBSTRUCTIVE SLEEP APNEA

Phase 2 study started by Merck



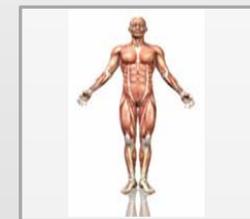
IPF COUGH

Phase 2 study conducted by Merck



ACUTE COUGH

Phase 2 study conducted by Merck

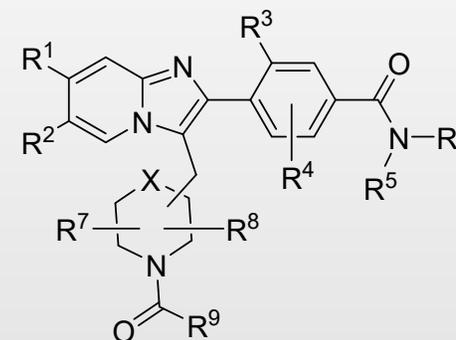


UNDISCLOSED INDICATION

Bellus preclinical studies ongoing

Inhibition of P2X3 receptors has therapeutic potential in a number of other indications

- Broad and comprehensive patent estate covering BLU-5937 and related compounds
- Composition of matter patent for BLU-5937 and related imidazopyridines granted in the U.S., Europe, Japan and China
- Long patent life, expiring in 2034 (not including potential patent term extension)



Composition of matter IP in place to 2034

Stock and Financial Information



\$35M Financing in December 2018



Ownership

~40%
institutional

~25%
founding
family offices

Company estimate based on financing participation, insider reporting and NOBO

Clean capital structure

158M basic shares
175M fully diluted shares

C\$48.9M / US\$35.9M

cash position¹ provides

~2

years of cash runway

¹as of December 31, 2018

Current cash provides ~2 years of capital through Phase 2

Past Execution

- ✓ BLU-5937 preclinical proof of concept (June 2017)
- ✓ \$20M financing (December 2017)
- ✓ BLU-5937 Phase 1 data with best in class taste profile (November 2018)
- ✓ \$35M financing (December 2018)



2019 Milestones

Execution of BLU-5937 plan in chronic cough:

- ✓ Phase 2 US Investigational New Drug (IND) and UK Clinical Trial Authorization (CTA) cleared (Q1 2019)
- Phase 1 abstracts accepted at American Thoracic Society Conference (May 21) and American Cough Conference (June 8)
- First patient dosed in Phase 2 (mid 2019)

Competitor Catalysts:

- Merck MK-7264 pipeline: Phase 2 in pain related to endometriosis (2H 2019)
- Bayer P2X3 Phase 1 and Phase 2 data

Important executional and value driving milestones in 2019



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