

Bellus
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Investor Presentation

NASDAQ/TSX - BLU

September 11, 2020

Forward Looking Statements

Certain statements contained in this presentation, other than statements of fact that are independently verifiable at the date hereof, may constitute “forward-looking statements” within the meaning of Canadian securities legislation and regulations and other applicable securities laws. Forward-looking statements are frequently, but not always, identified by words such as “expects,” “anticipates,” “believes,” “intends,” “estimates,” “potential,” “possible,” “projects,” “plans,” and similar expressions. Such statements, based as they are on the current expectations of management, inherently involve numerous important risks, uncertainties and assumptions, known and unknown, many of which are beyond BELLUS Health’s control. Such statements include, but are not limited to, the potential of BLU-5937 to successfully treat chronic cough, chronic pruritus and other hypersensitization-related disorders, BELLUS Health’s expectations related to its preclinical studies and clinical trials, including the timing of initiation and completion of and results from the BLU-5937 Phase 2 RELIEF trial and its chronic pruritus program, the potential tolerability profile and other characteristics of BLU-5937 as compared to other competitor candidates and the potential applicability of BLU-5937 and BELLUS Health’s P2X3 platform to treat other disorders. Risk factors that may affect BELLUS Health’s future results include but are not limited to: the ability to expand and develop its project pipeline, the ability to obtain adequate financing, the ability of BELLUS Health to maintain its rights to intellectual property and obtain adequate protection of future products through such intellectual property, the impact of general economic conditions, general conditions in the pharmaceutical industry, the impact of the COVID-19 pandemic on BELLUS Health’s operations, plans and prospects, including to the initiation and completion of clinical trials in a timely manner or at all, changes in the regulatory environment in the jurisdictions in which BELLUS Health does business, stock market volatility, fluctuations in costs, changes to the competitive environment due to consolidation, achievement of forecasted burn rate, potential payments/outcomes in relation to indemnity agreements and contingent value rights, achievement of forecasted preclinical study and clinical trial milestones, reliance on third parties to conduct preclinical studies and clinical trials for BLU-5937 and that actual results may vary once the final and quality-controlled verification of data and analyses has been completed. In addition, the length of BELLUS Health’s product candidate’s development process and its market size and commercial value are dependent upon a number of factors. Moreover, BELLUS Health’s growth and future prospects are mainly dependent on the successful development, patient tolerability, regulatory approval, commercialization and market acceptance of its product candidate BLU-5937 and other products. Consequently, actual future results and events may differ materially from the anticipated results and events expressed in the forward-looking statements. BELLUS Health believes that expectations represented by forward-looking statements are reasonable, yet there can be no assurance that such expectations will prove to be correct. The reader should not place undue reliance, if any, on any forward-looking statements included in this presentation. These forward-looking statements speak only as of the date made, and BELLUS Health is under no obligation and disavows any intention to update publicly or revise such statements as a result of any new information, future event, circumstances or otherwise, unless required by applicable legislation or regulation.

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Company Overview

BELLUS Overview

BLU-5937 – Highly Selective P2X3 Antagonist for Hypersensitization Disorders

Lead Indication - Refractory Chronic Cough

- Large population, 9m in U.S., with significant unmet need
- BLU-5937, a second generation highly selective P2X3 antagonist, has shown reduction in cough frequency in patients ≥ 20 coughs/h and low taste side effects
 - First generation P2X3 antagonist in Phase 3, Merck's MK-7264: efficacious but has taste alteration/loss in 58-69% of patients¹
- Phase 2b trial expected to start in Q4 2020

Pipeline within a Molecule

- Potential for broad applicability in hypersensitization disorders
- 5 non-cough indications in phase 2 with P2X3 antagonists expected in 2020 including phase 2 with BLU-5937 for chronic pruritus²

Well Financed

~\$74M³ cash position

100% Owned Composition of Matter IP

100% owned patent estate including composition of matter covering BLU-5937 expiring in 2034

¹McGarvey L., Two Phase 3 Randomized Clinical Trials of Gefapixant, a P2X3 Receptor Antagonist, in Refractory or Unexplained Chronic Cough (COUGH-1 and COUGH-2), ERS Abstract 2020

²4 indications (pain related to endometriosis, overactive bladder, sleep apnea and neuropathic pain) in development by third parties

³as of June 30, 2020

Strong Leadership and Advisory Group

Management



Roberto Bellini
President & Chief Executive Officer



Dr. Catherine Bonuccelli
Chief Medical Officer



Dr. Denis Garceau
Senior Vice President, Drug Development



François Desjardins
Vice President, Finance



Tony Matzouranis
Vice President, Business Development

Board of Directors



Dr. Francesco Bellini
Chair



Franklin Berger



Roberto Bellini



Dr. Clarissa Desjardins



Dr. Youssef Bennani



Pierre Larochelle



Joseph Rus

Clinical Advisory Board

Dr. Jacky Smith (Chair), MB, ChB, FRCP, PhD
University of Manchester

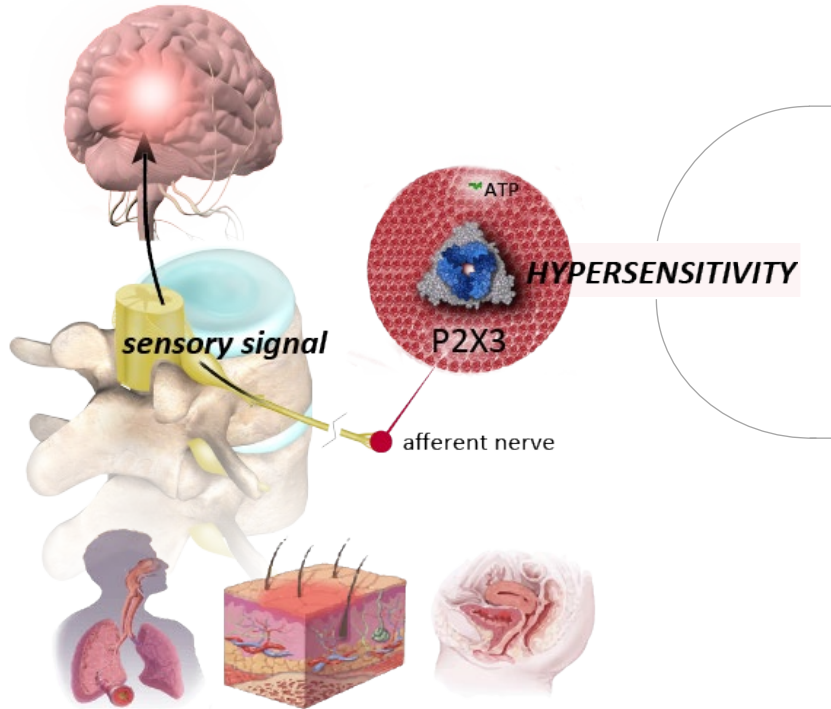
Dr. Michael S. Blaiss, MD
Medical College of Georgia

Dr. Surinder Biring, MB ChB (Hons), MD
Kings College London

Dr. Peter Dicipinigaitis, MD
Albert Einstein Medical College

P2X3 Linked to Cough & Other Hypersensitization Disorders

P2X3 is an ATP gated ion channel in the peripheral sensory nervous system



PRIMARY IRRITATIVE SYMPTOMS

Chronic Cough

- **Urge to cough**

Other Hypersensitization Disorders

- Urge to scratch
- Pain
- Allodynia
- Allotussia
- Irritation

SECONDARY AUTONOMIC REFLEXES

Chronic Cough

- **Cough**

Other Hypersensitization Disorders

- Scratching
- Overactive bladder
- Hypertension
- Hyperreflexia carotid body
- GI hyperactivity

BLU-5937: Pipeline Within a Molecule

PROGRAM	DEVELOPMENT				STATUS	
Indication	Preclinical	phase 1	phase 2	phase 3	Worldwide Rights	Next Anticipated Milestone
BLU-5937						
Refractory Chronic Cough					Bellus HEALTH	Q4 2020: FDA meeting and phase 2b start
Chronic Pruritus Associated with Atopic Dermatitis					Bellus HEALTH	Q4 2020: phase 2 start

Potential for Broad Applicability and Building Pipeline in a Product

PH2 TRIALS ONGOING OR PLANNED IN 5 NON-COUGH P2X3 INDICATIONS



- CHRONIC PRURITUS



- SLEEP APNEA
- ENDOMETRIOSIS PAIN



- SLEEP APNEA
- NEUROPATHIC PAIN



- OVERACTIVE BLADDER



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Refractory Chronic Cough

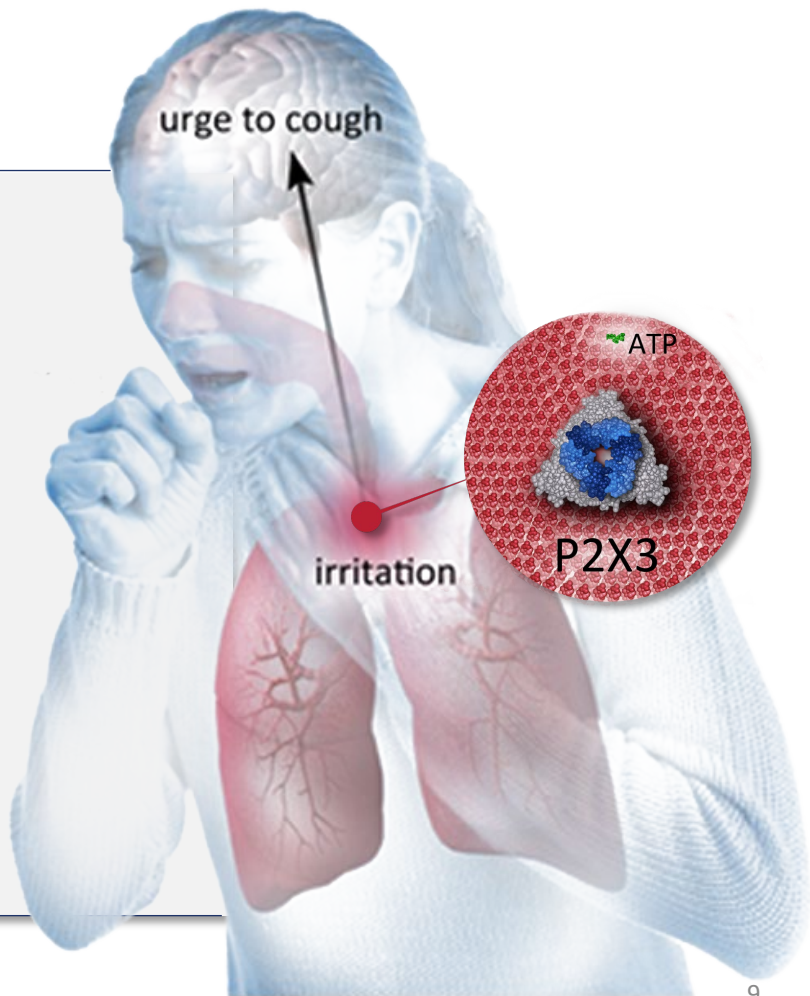
Refractory Chronic Cough

Cough lasting ≥ 8 weeks that does not respond to treatment for underlying cause or is unexplained

Significant impact on patients' quality of life including impact on social, physical and psychosocial well-being

Current treatment options are inadequate and non-specific

Large patient population¹ - up to ~9M refractory chronic cough patients in the U.S. with ~3M patients coughing >1 year



Proof-of-Mechanism Illustrated by First-in-Class P2X3 Antagonist MK-7264

MK-7264



First generation P2X3
antagonist with low
selectivity

**Effective in reducing
cough but with
Taste Side Effects**

Two Phase 3 Trials of Gefapixant: COUGH-1 (12 week duration) and COUGH-2 (24 week duration)

Cough

18% & 15%

placebo adjusted
reduction in 24H
cough frequency
(primary endpoint)

Taste

58% & 69%

of patients have
taste alteration
or taste loss

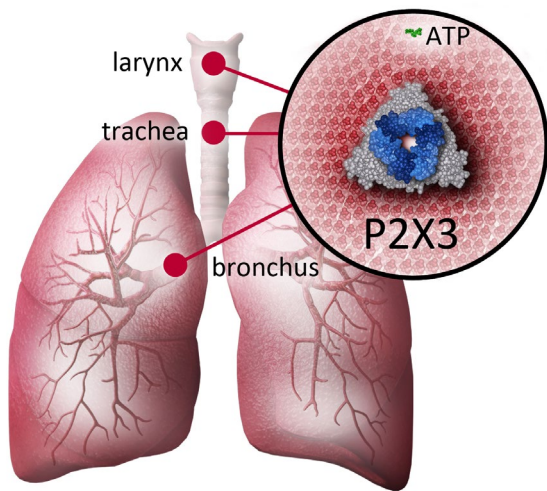
McGarvey L., Two Phase 3 Randomized Clinical Trials of Gefapixant, a P2X3 Receptor Antagonist, in Refractory or Unexplained Chronic Cough (COUGH-1 and COUGH-2), ERS Abstract 2020; 45mg BID dose data presented

Lack of P2X3 Selectivity Results in Taste Effect

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

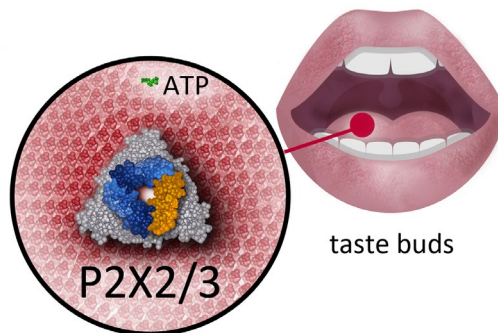
COUGH REFLEX:

P2X3 **homotrimers** have primary role in cough



TASTE:

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



OPPORTUNITY:

Highly selective P2X3 antagonist to reduce cough (P2X3 inhibition) and maintain taste (no P2X2/3 inhibition)

BLU-5937: P2X3 Antagonist with Best in Class Selectivity

BLU-5937

HIGHLY POTENT¹

P2X3 antagonist
Low nM IC₅₀

CLINICALLY MEANINGFUL²

reduction in cough frequency
in RCC patients ≥20 coughs/h

HIGHLY SELECTIVE¹

P2X3 antagonist
~ 1500X selectivity vs P2X2/3

WELL TOLERATED

Low taste side effects (≤10%)



SELECTIVITY

3-7x³

17-126x⁴

~250x⁵

1500x

¹IC₅₀ calculated using cloned hP2X3 and hP2X2/3 channels expressed in HEK295 cells; (Ca²⁺ FLIPR)

²BELLUS RELIEF Phase 2 Trial Results





³Smith J., Lancet Respir Med 2020: Gefapixant, a P2X3 receptor antagonist, for the treatment of refractory or unexplained chronic cough: a randomised, double-blind, controlled, parallelgroup, phase 2b trial

⁴Bayer selectivity range of most characterized P2X3 antagonists described in Bayer US patent 10,183,937 (may not be BAY1817080)

⁵Niimi A, European Respiratory Journal 2019 54: RCT452

P2X3 Competitive Landscape¹

Best in class selectivity for P2X3 supports potential favorable clinical and commercial profile

	1 ST IN CLASS P2X3 ANTAGONIST	2 ND GENERATION P2X3 ANTAGONISTS		BEST IN CLASS SELECTIVITY FOR P2X3
Company	 MERCK			
Candidate	MK-7264 ²	BAY 1817080 ³	S-600918 ⁴	BLU-5937
Trial	phase 3	phase 2	phase 2	phase 2
Trial ID(s)	NCT03449147 / NCT02612623	NCT03310645	JAPIC-CTI184027	NCT03979638
Dosing	BID	BID	QD	BID
P2X3 vs. P2X2/3 Selectivity	3-7x	17-126x ⁵	~ 250x	~ 1500x

¹No head to head clinical trials have been conducted; data derived from different clinical trials in different patient populations and with different dosing regimes and protocols.

²McGarvey L, Two Phase 3 Randomized Clinical Trials of Gefapixant, a P2X3 Receptor Antagonist, in Refractory or Unexplained Chronic Cough (COUGH-1 and COUGH-2), ERS Abstract 2020

³All BAY 1817080 data except selectivity from ATS 2020 Abstract A7648. Safety and Efficacy of BAY 1817080, a P2X3 Receptor Antagonist, in Patients with Refractory Chronic Cough

⁴All S-600918 data from phase 2a Presentation, ERS, September 29, 2019

⁵Bayer selectivity range of most characterized P2X3 antagonists described in Bayer US patent 10,183,937 (may not be BAY1817080)

Phase 2 RELIEF Trial Design

(A Randomized, Double-blind, Placebo-Controlled, Crossover, Dose Escalation Study of BLU-5937 in Subjects with Unexplained or Refractory Chronic Cough)

Primary endpoint:

Placebo-adjusted reduction in awake cough frequency using cough recorder

68 refractory chronic cough patients:

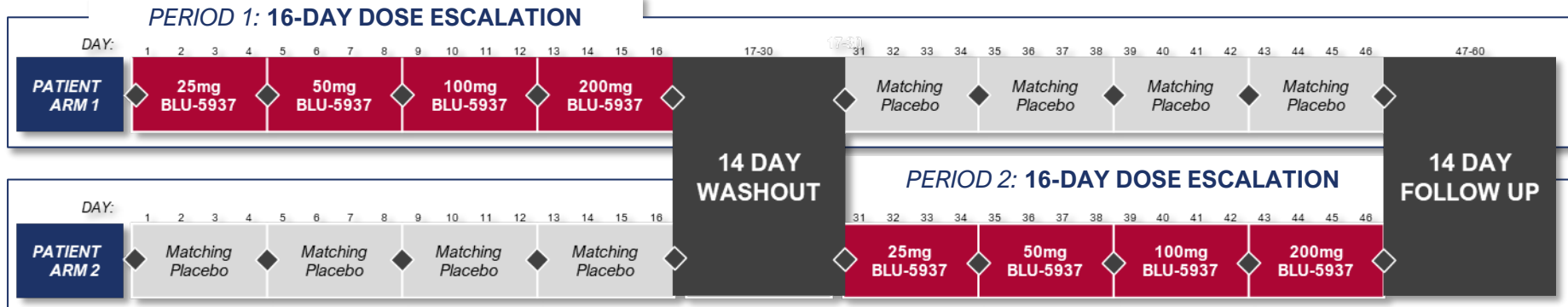
- 52 completed dosing
- 13 pandemic-related discontinuations
- 3 non-drug related discontinuations

16 sites in UK and US:

- 40 patients from 8 UK sites
- 28 patients from 8 US sites

4 dose levels:

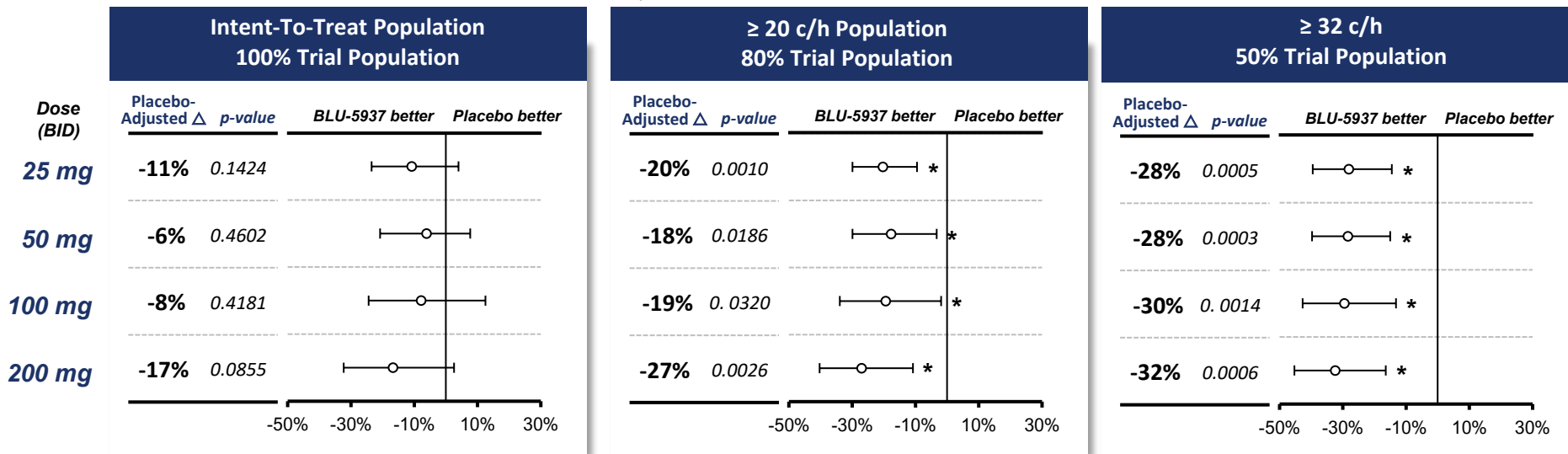
- 25/50/100/200mg BID with forced dose escalation at 4-day intervals



BLU-5937: RELIEF PHASE 2 TRIAL PRIMARY ENDPOINT

- RELIEF trial achieved similar magnitude of effect to Merck Phase 3 trials but did not achieve statistical significance in the overall population
- In pre-specified subgroup analyses of patients with ≥ 20 coughs/h and 32 coughs/h, statistically significant reductions in awake cough frequency were achieved at all doses
 - ≥ 20 c/hr : 18-27% placebo-adjusted reduction in awake cough frequency ($p < 0.032$)
 - ≥ 32 c/hr : 28-32% placebo-adjusted reduction in awake cough frequency ($p < 0.0015$)

PLACEBO-ADJUSTED CHANGE IN AWAKE COUGH FREQUENCY



Key learning that baseline cough frequency is an important indicator of treatment benefit

BLU-5937 RELIEF Phase 2 and MK-7264 Phase 3 Trial

Intent-To-Treat Population



BLU-5937¹

RELIEF: Phase 2 (4 days)
200mg BID

31/26 c/h

**Baseline Awake Cough
Frequency**

17%

**Placebo Adjusted
Reduction in Awake
Cough Frequency**

9%

Taste AEs



MK-7264² (gefapixant)

COUGH-1: Phase 3 (12-wk)
45mg BID

25-30 c/h

**Baseline Awake Cough
Frequency**

18%

**Placebo Adjusted
Reduction in Awake
Cough Frequency**

58%

Taste AEs



MK-7264² (gefapixant)

COUGH-2: Phase 3 (24-wk)
45mg BID

24-26 c/h

**Baseline Awake Cough
Frequency**

16%

**Placebo Adjusted
Reduction in Awake
Cough Frequency**

69%

Taste AEs

- Similar magnitude of placebo-adjusted effect with significant reduction in taste effect with BLU-5937 though comparison limited by:
 - Trial design (crossover vs parallel arm)
 - Duration of trial (16 days drug; 4 days 200mg BID vs 12/24 weeks)
 - Differences in baseline cough frequency
 - Differences in placebo effects

No head-to-head clinical trials have been conducted; data derived from different clinical trials in different patient populations and with different dosing regimens and protocols.

¹RELIEF Phase 2 Trial data including geometric mean for baseline awake cough frequency (period 1 and period 2)

²McGarvey L., Two Phase 3 Randomized Clinical Trials of Gefapixant, a P2X3 Receptor Antagonist, in Refractory or Unexplained Chronic Cough (COUGH-1 and COUGH-2), ERS Abstract 2020

BLU-5937 RELIEF Phase 2 and S-600918 Phase 2 Trial

Similar reduction in awake cough frequency using populations with similar baseline cough frequency



BLU-5937 phase 2
≥ 32 coughs/h Patients¹
25-200mg BID

55/59 c/h
Baseline Cough Frequency²

28-32%
Placebo Adjusted
Reduction in Awake
Cough Frequency



S-600918 phase 2A
150mg QD

56 c/h
Baseline Cough Frequency²³

32%
Placebo Adjusted
Reduction in Awake
Cough Frequency²

Ishihara et al. ERS2020 PA2271: *“Design of phase 2b randomised controlled trial of S-600918, P2X3 receptor antagonist for refractory chronic cough”*

- Interaction between baseline cough frequency and treatment effect observed in Phase 2a trial
- Phase 2b Design:
 - Enrichment strategy with baseline cough frequency inclusion criteria, ≥10 coughs/h (24-hours)
 - Patient stratification by baseline cough frequency to help balance trial arms

Interaction between baseline cough frequency and treatment effect observed in RELIEF and Shionogi Phase 2 trials

No head-to-head clinical trials have been conducted; data derived from different clinical trials in different patient populations and with different dosing regimens and protocols.



¹ Pre-specified sub-group analysis of RELIEF Phase 2 trial

² Shionogi: not disclosed if arithmetic or geometric mean; Bellus: both arithmetic and geometric means presented

³ Niimi A et al. ; Eur.Respir. J 2019 54: Suppl. 63, RCT452

RELIEF: Well-Tolerated and Safety Profile Comparable to Placebo

INCIDENCE OF MOST FREQUENT ADVERSE EVENTS (>5% INCIDENCE)

	Placebo (N=61)	BLU-5937 Total (N=61)
n of subjects (%) with Adverse Events	41 (67.2%)	42 (68.9%)
Serious Adverse Events	0	0
Most Common TEAEs (≥5% of subjects)		
Headache	7 (11.5%)	6 (9.8%)
Back pain	6 (9.8%)	5 (8.2%)
Dysgeusia	2 (3.3%)	5 (8.2%)
Diarrhea	3 (4.9%)	4 (6.6%)
URTI	3 (4.9%)	4 (6.6%)
Dizziness	2 (3.3%)	4 (6.6%)
Oropharyngeal pain	0 (0%)	3 (4.9%)

- Similar incidence of adverse events on placebo and active
- No serious adverse events
- No clinically significant effect on vital signs, ECG and laboratory measures
- Low incidence of potential P2X3 class-related side effects (taste effects, hypoaesthesia)
- No drug-related discontinuations

RELIEF: Taste Disturbance Adverse Events

Low incidence and mild nature of taste side effect at all doses:

- No complete loss of taste at any dose
- No dropouts due to taste disturbance
- Only 2 cases of partial taste loss
- Mostly mild in nature

*INCIDENCE OF TASTE DISTURBANCE ADVERSE EVENTS
ITT POPULATION*

	Placebo (n=61)	25mg BID (n=61)	50mg BID (n=61)	100mg BID (n=59)	200mg BID (n=58)	Total BLU- 5937 (n=61)
Taste Disturbance	2 (3.3%)	3 (4.9%)	5 (8.2%)	5 (8.3%)	4 (6.9%)	5 (8.2%)
Partial Taste Loss	1 (1.6%)	2 (3.3%)	2 (3.3%)	2 (3.4%)	2 (3.4%)	2 (3.3%)
Complete Taste Loss	0	0	0	0	0	0
Total Taste AEs	3 (4.9%)	4 (6.5%)	6 (9.8%)	6 (10.0%)	5 (8.6%)	6 (9.8%)

BLU-5937: Favorable Drug Profile



- **Favorable efficacy and safety profile**
- **Efficient development path moving forward**
- **Twice daily dosing with potential to achieve once-daily**
- **Best in class selectivity**
- **Favorable drug characteristics:**
 - DDI unlikely
 - No food effect
 - No off-target adverse effects identified



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SOOTHE Phase 2b Trial Design & RCC Commercial Considerations

Learnings from RELIEF Trial for Phase 2b Design

- Cough frequency at baseline is a key indicator of treatment benefit with ≥ 20 coughs/h demonstrating statistically significant and clinically meaningful benefit
- Patient level data between 20-32 coughs/h



- 25 coughs/h cutoff selected for Phase 2b population

- 200 mg BID dose slightly outperformed other doses but cannot distinguish effect of dose level from duration of treatment
- Plasma concentrations achieved in RELIEF are consistent with achieving receptor occupancies in the 75-95+% range
- Within-patient dose response curves are shallow with overall effect size increasing with increasing baseline cough frequency

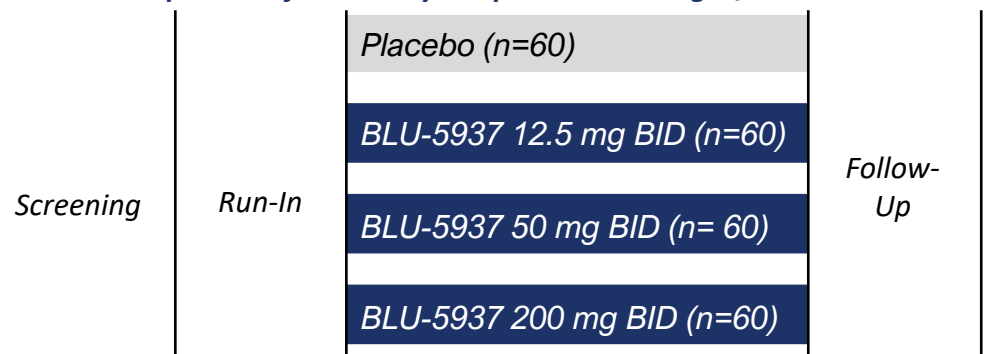


- 12.5mg, 50mg and 200mg BID selected as doses

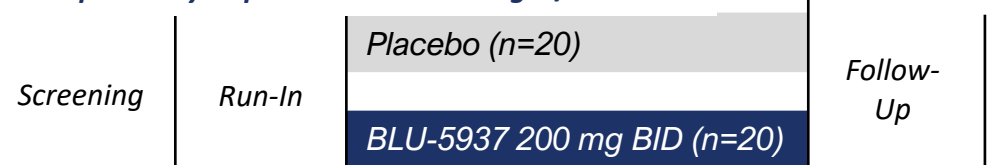
SOOTHE Phase 2b – Expected Trial Design

Randomized, double-blind, 4-week placebo-controlled parallel arm study with 3 active doses

— Main Population for Primary Endpoint - ≥ 25 coughs/hr



— Exploratory Population - 10-25 coughs/hr



Days: -14 — -7 — 0 ————— 29 ————— 43

24H Cough recordings: ♦ ♦ ♦ ♦

ENDPOINTS

Primary: **Change from baseline in 24H cough frequency** using cough recorder in ≥ 25 coughs/h population

Key Secondary: Change from baseline in awake cough frequency, Leicester Cough Questionnaire and Cough Severity Visual Analogue Scale

MAIN POPULATION

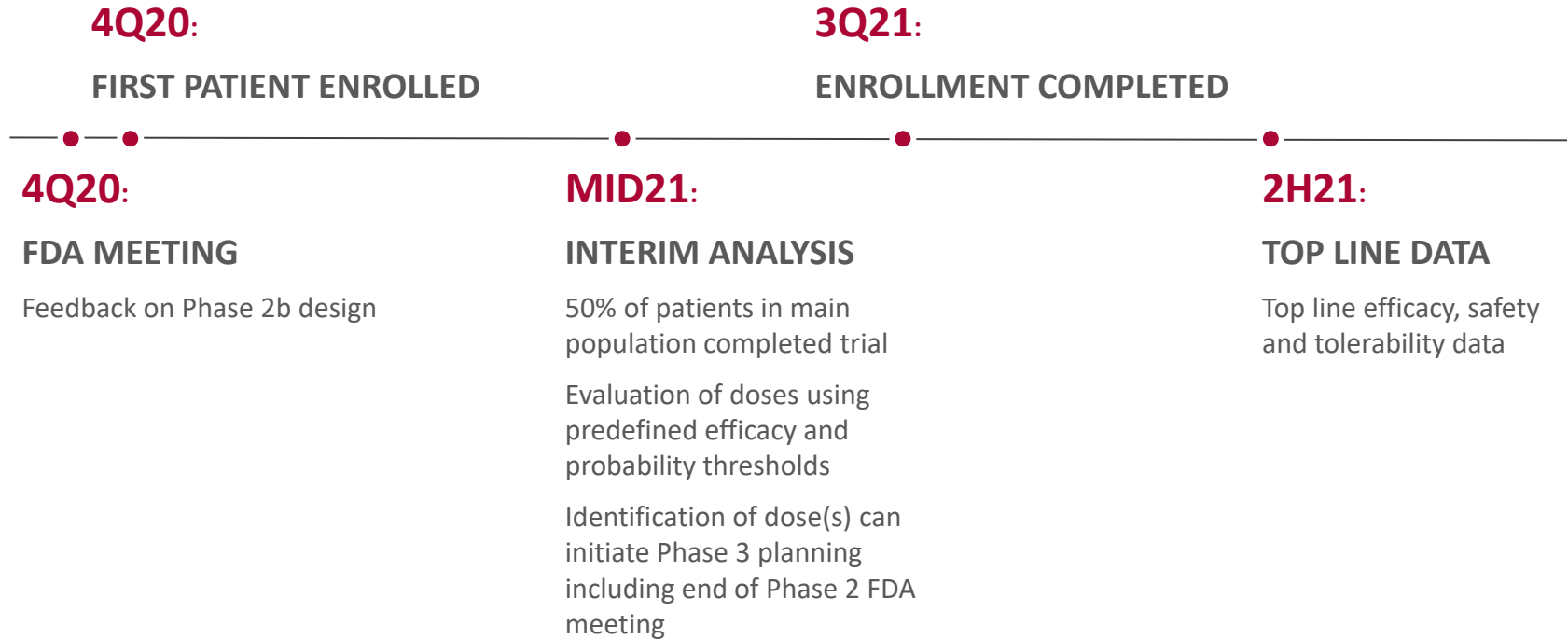
Diagnosed refractory chronic cough >1 year

Screening and baseline awake cough frequency ≥ 25 coughs/h using cough recorder

SITES

Approximately 100 sites: ~50% US / ~50% ex-US

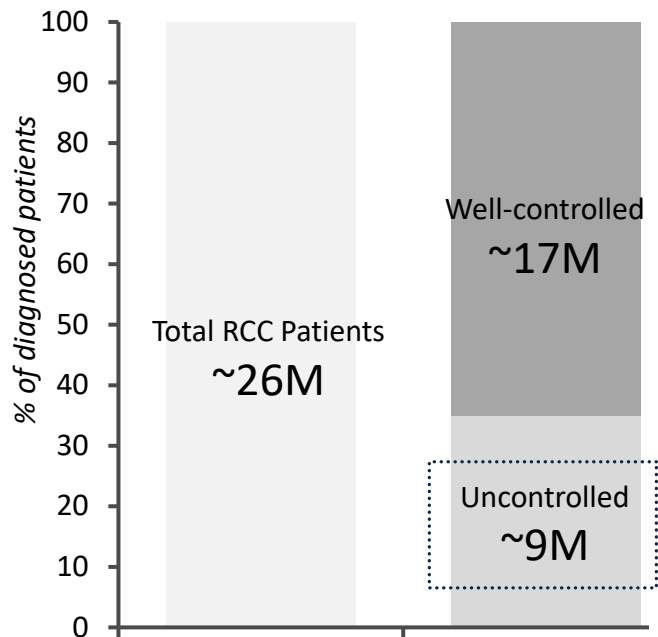
SOOTHE Phase 2b – Expected Timeline



Chronic Cough Patient Population

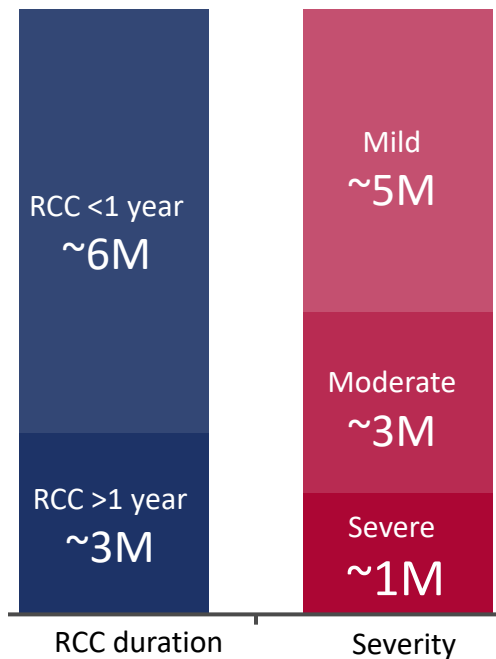


Chronic cough patient segmentation¹ (2020E)



BLU-5937: Expected addressable patient population

US Market: ~9M



Mild

Daily cough symptoms with mild disturbance to QoL
Few adverse effects (e.g., depression, incontinence, sleep deprivation, etc.)

Moderate

Frequent coughing causing lifestyle alteration.
Adverse effects include mild depression, anxiety and fragmented sleep.

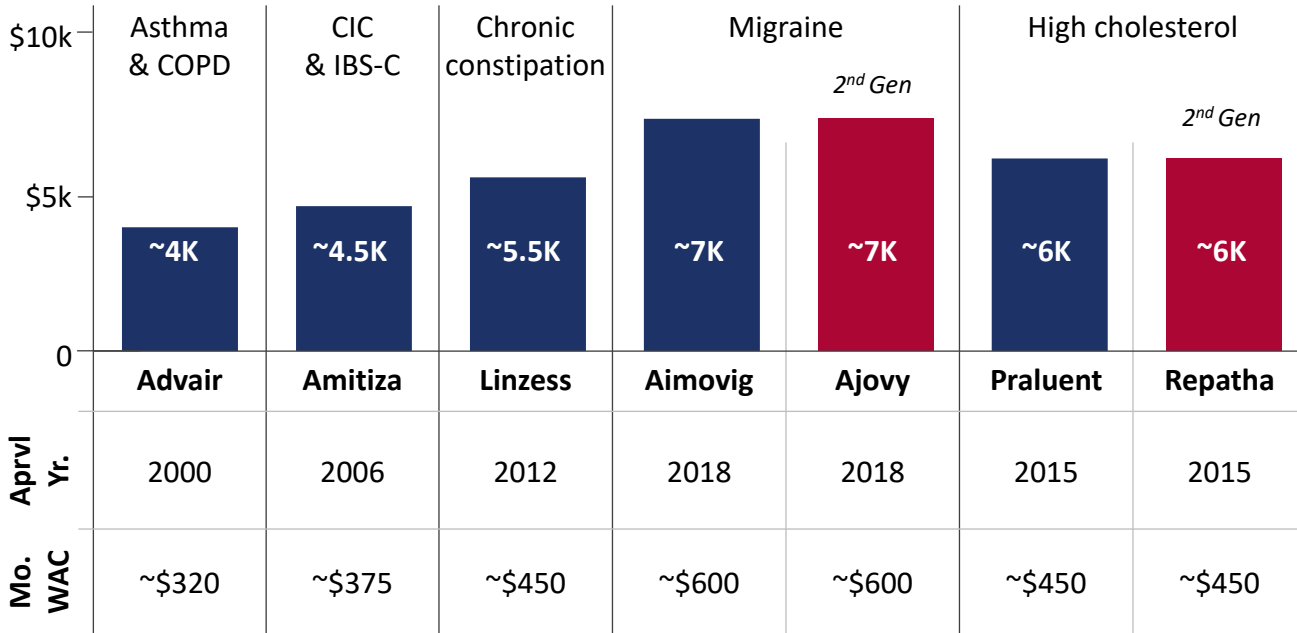
Severe

Intense coughing episodes causing significant discomfort and distress Prevents ability to sleep, work, and/or socialize.

P2X3 Class and BLU-5937: Pricing Comparables

Annual WAC cost of analogue drugs

Thousands of USD (2020)



PRICING COMPARABLES

- Pricing analogues provide range of \$300-600 WAC per month

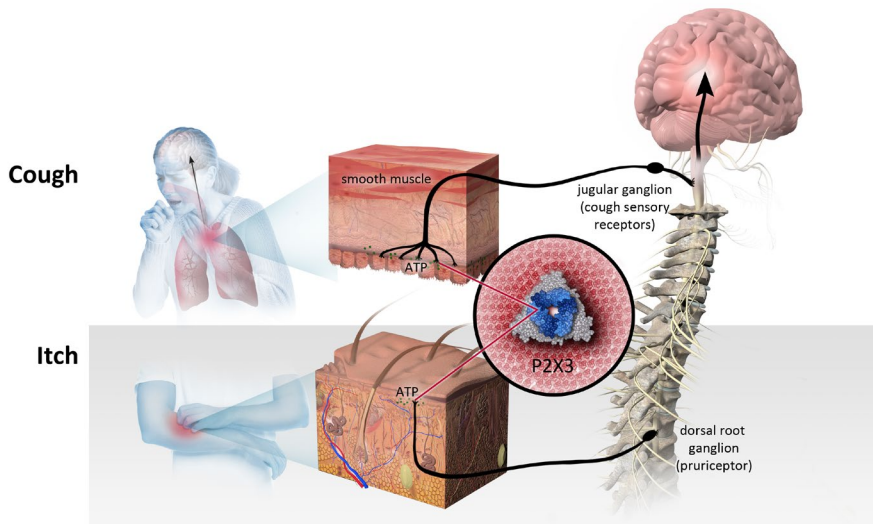


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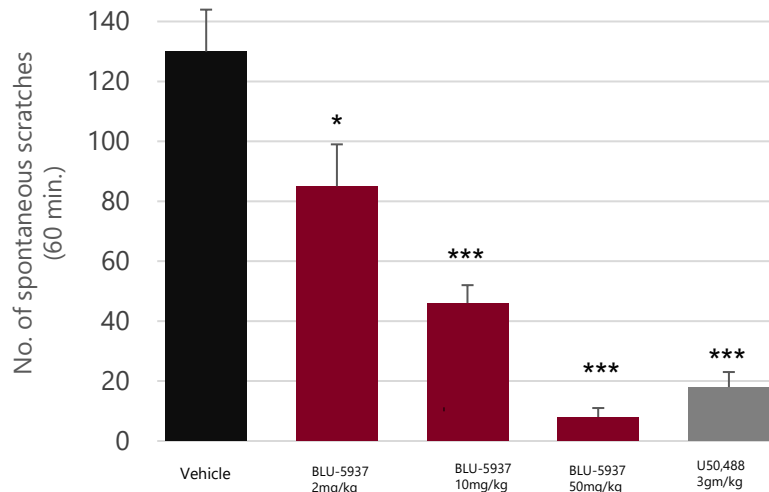
BLU-5937: Beyond Chronic Cough

BLU-5937 Second Indication: Chronic Pruritus Associated with Atopic Dermatitis

Mechanistic Similarities Between Cough and Itch



Animal POC – Atopic Dermatitis Mouse Model

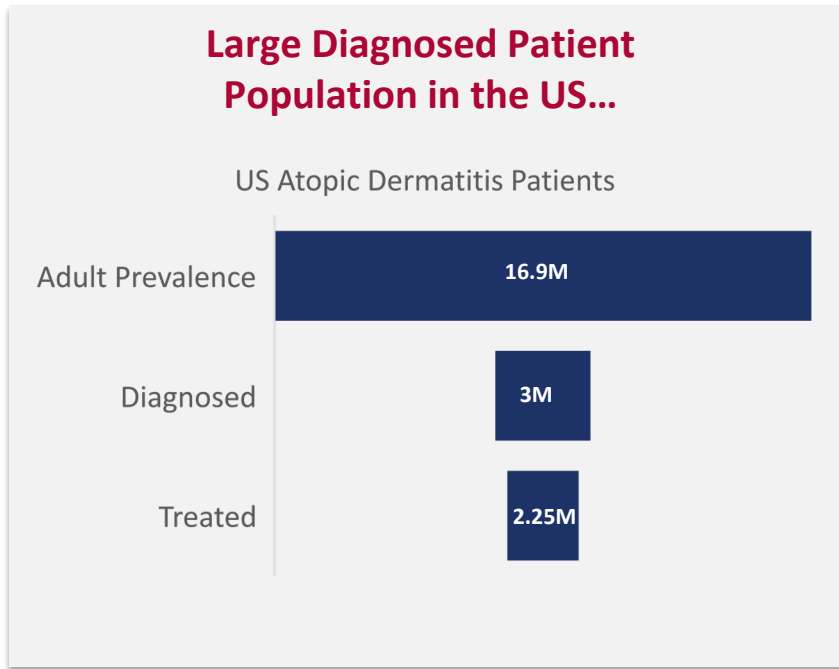


Chauret et al. 2019 J Invest. Derm. 139 (9) S232, 106: Number of spontaneous scratches in 60 min of day 8 Calcipotriol (MC903) treated mice pre-injected with vehicle, 2, 10, or 50 mg/kg test BLU-5937, or 3 mg/kg U50,488. (n = 10 mice per group), *p < 0,05, ***p < 0.0001, one-way ANOVA. Data are represented as mean ± S.E.M. U50,488: kappa opioid agonist

Mechanistic rationale and preclinical data support moving into the clinic

AD Chronic Pruritus Market

Large Diagnosed Patient Population in the US...



...with 40-50% Patients Having Residual Itch

Limitations of Current Therapies

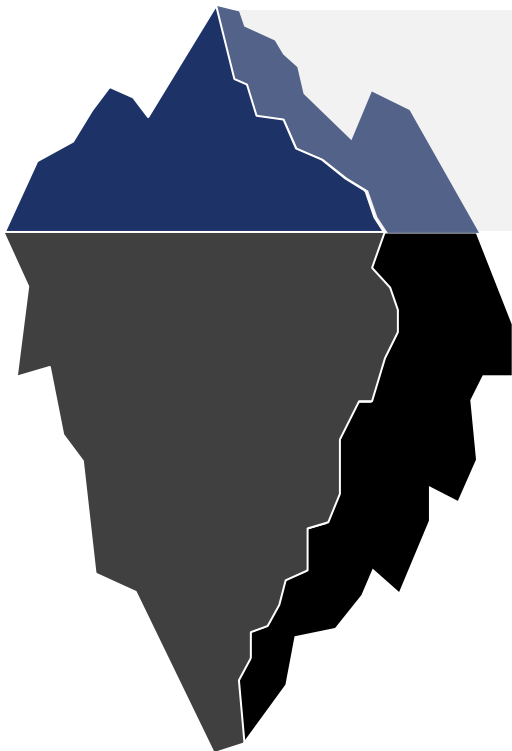
Corticosteroids	Significant side effects
Antihistamines	Limited effect
Immuno-suppressants	Toxicity
Dupixent	Cost & low reimbursement rate

Report 2019 Bluestar BioAdvisors

Phase 2 proof of concept trial in ~100 mild/moderate atopic dermatitis patients with moderate/severe chronic pruritus expected to start in 4Q 2020

Potential for Broad Applicability Across Important Markets

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



REFRACTORY CHRONIC COUGH

- ~10% global prevalence for Chronic Cough¹
- ~3M US adults with refractory chronic cough >1 year; ~6M US adults with RCC <1 year¹

CHRONIC ITCH ASSOCIATED WITH ATOPIC DERMATITIS

- ~17m US adults suffer from atopic dermatitis¹

ENDOMETRIAL-RELATED PAIN

- Affects ~4m women in the United States¹
- MK-7264 Ph2 on-going²

SLEEP APNEA

- Affects ~23m in the United States¹
- S-600918 Ph2 initiated³

OVERACTIVE BLADDER

- Affects ~33m in the United States¹
- BAY 1817080 Ph2 initiated⁴

NEUROPATHIC PAIN

- Affects ~20m in the United States¹
- S-600918 Ph2 initiated³

OTHER POTENTIAL INDICATIONS

- Migraine
- Hypertension
- IBS
- Bladder Pain
- Bronchoconstriction

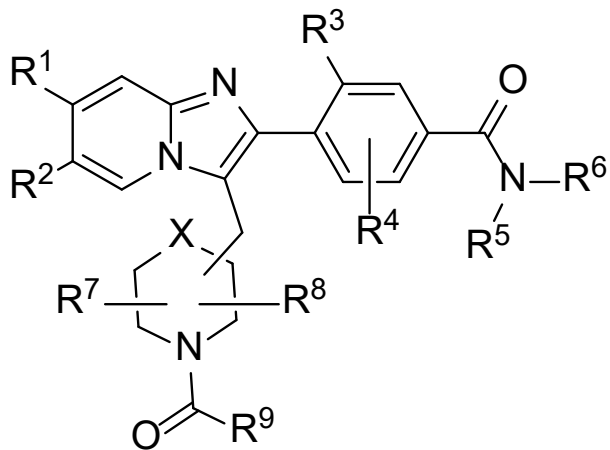


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IP and Corporate Summary

100% Owned Intellectual Property Portfolio

Composition of matter patent expires in 2034



- All intellectual property 100% owned with no future obligations owed
- U.S. and international patent estate covering BLU-5937 and related compounds
- Composition of matter patent for BLU-5937 and related P2X3 antagonists granted in the U.S., Europe, Japan, and China (expires in 2034 not including potential patent term extension)
- Methods of Use patent for the treatment of cough granted in the U.S. (expires 2038)

Stock and Financial Information

Capital Structure¹

60.4M basic shares

66.1M fully diluted shares

¹ as of August 12, 2020

Cash Position²

Cash, cash equivalents, and short-term investments
position of \$74M²

² as of Jun 30, 2020

Potential Catalysts & Upcoming Events

Key Anticipated Milestones in 2020 and 2021

BLU-5937 in chronic cough:

- ✓ BLU-5937 KOL Event in Chronic Cough (May 27, 2020)
- ✓ RELIEF Phase 2 top-line data
- ✓ Phase 2b trial design (3Q20)
 - Regulatory feedback (4Q20)
 - SOOTHE Phase 2b trial initiation (4Q20)
 - Respiratory/cough conferences: ERS (September) and ICS (January 2021)

BLU-5937 in chronic pruritus associated with AD

- Phase 2 design and first patient enrolled (2H20)

Other P2X3 trials

- Phase 2 on-going in overactive bladder, neuropathic pain, pain-related to endometriosis and sleep apnea

Recent competitor data:



September 7th-9th, 2020

- **Shionogi:** Design of a Ph2b randomised control trial of S-600918¹
- **Bayer:** Safety & Efficacy of BAY1902607 in RCC¹
- **Merck:** Two Phase 3 Randomized Clinical Trials of Gefapixant, Refractory or Unexplained Chronic Cough (COUGH-1 and COUGH-2)¹

¹ 2020 - ERS International Congress - European Respiratory Society (www.erscongress.org)