Improvements in Cough Severity and Quality of Life in SOOTHE, A Phase 2b, Dose Finding Trial of BLU-5937 in Refractory Chronic Cough

Birring S. S[1], Smith J[2], Morice A. H[3], McGarvey L[4], Sher M. R[5], Goldsobel A. B[6], Lanouette S[7], Harvey L[7], Yang R[8], Garin M[8], Bonuccelli C. M[8]

1.Kings College Hospital, London, UK, 2.Manchester University NHS Foundation Trust, Manchester, UK, 3.University of Hull, Cottingham, UK, 4.Queen's University Belfast, Belfast, UK, 5.Center for Cough, Largo, FL, USA, 6.Allergy and Asthma Assoc of N California, San Jose, CA, USA, 7.Bellus Health, Laval, QC, Canada, 8.Bellus Health, Wilmington, DE, USA

Introduction

- Refractory Chronic Cough (RCC) is a cough that persists for 8 weeks or more despite adequate treatment of all identifiable associated diseases or without identifiable cause[1,2].
- The current lack of approved treatment exacerbates the significant physical, psychological, and social burdens RCC imposes on patients.

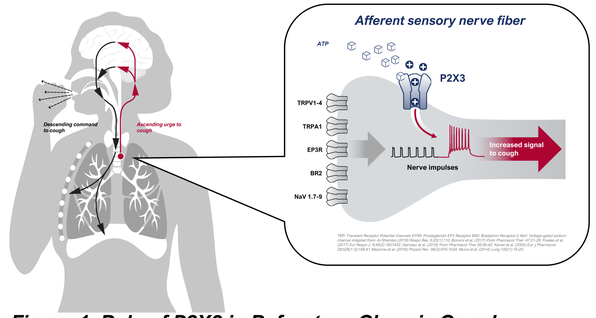

Figure 1. Role of P2X3 in Refractory Chronic Cough

- The ATP-gated ion channel P2X3 is suggested to play a role in the pathophysiology of RCC (Fig. 1), and P2X3 antagonists have shown promise as a treatment for RCC[3-5].
- We report the improvement in patient-reported outcomes from a phase 2b study in RCC of BLU-5937, a highly selective P2X3 antagonist, for the treatment of RCC.

Methodology

- SOOTHE (NCT04678206) was a multi-center Phase 2b, randomized, placebo-controlled, parallel arm, clinical dose-finding study in participants diagnosed with RCC for ≥1 year.

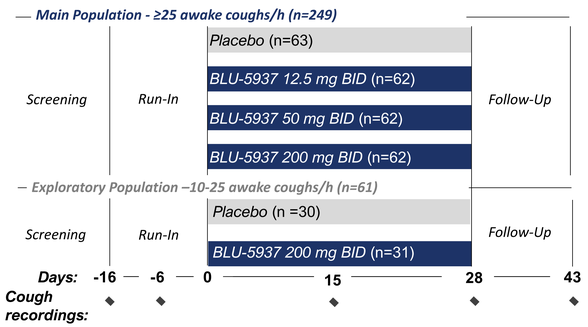

Figure 2. SOOTHE Study Design

- The primary endpoint was the change from baseline in 24H cough frequency.
- Following a single-blind run-in period, 249 participants who had maintained a baseline awake cough frequency ≥25 coughs/h were randomized 1:1:1:1 to the three active treatment arms of BLU-5937 (12.5, 50 and 200 mg BID) or placebo for 4 weeks of double-blind treatment.

Results

24H Cough Frequency

- In SOOTHE, statistically significant reductions in change in 24-hour cough frequency over placebo were observed at Days 15 and 28 with treatment with BLU-5937 50 and 200 md BID (Fig. 3).
- A dose response was observed between the 12.5 mg and 50 mg BID doses.

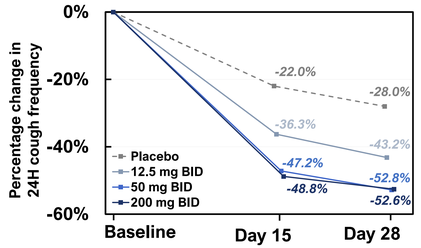

Figure 3. Change From Baseline In 24H Cough Frequency

Leicester Cough Questionnaire

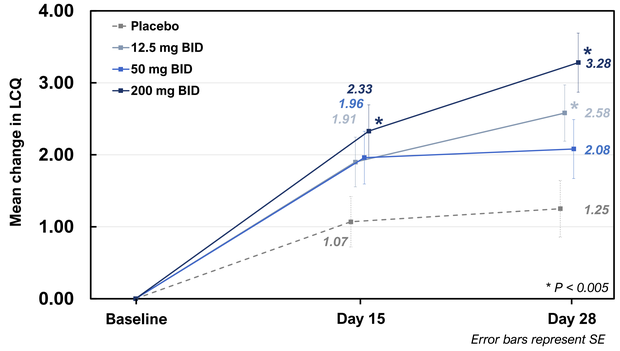

Figure 4. Change From Baseline in Leicester Cough Questionnaire

- Cough-specific quality of life was assessed using the Leicester Cough Questionnaire (LCQ). The questionnaire reflects the impact of cough on quality of life on a scale from 3 to 21. Higher scores represent a better quality of life.
- Participants treated with BLU-5937 demonstrated improvements in the impact of cough on their quality of life, as measured by the LCQ, all above the MCID of 1.3-point.
- Participants treated with 12.5, 50 and 200 mg BID or placebo demonstrated mean improvements from baseline in LCQ score after 28 days of 2.58, 2.08, 3.38 and 1.25 points, respectively (Fig 4).
- SOOTHE was not powered to observe a difference in LCQ scores. Nonetheless, significant difference from placebo in change from baseline in LCQ score were observed for 200 mg BID at Days 15 and D28 and for 12.5 mg BID at D28 (Fig. 4).

Cough Severity Visual Analog Scale

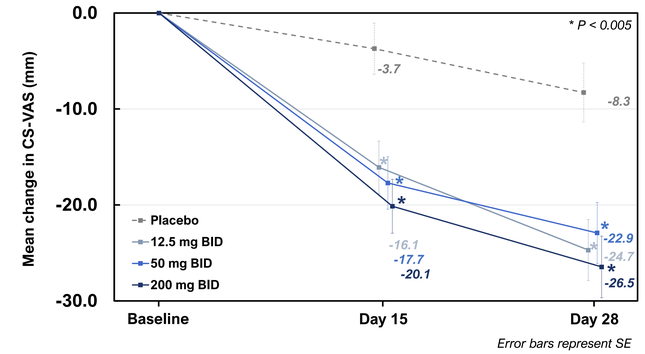

Figure 5. Change From Baseline in Cough-Severity VAS

- Cough severity was assessed using the Cough Severity Visual Analogue Scale (CS-VAS). Scores range from 0 to 100mm with 0 mm representing no cough and 100 mm the worst imaginable cough.
- All doses reached statistical significance ($p \leq 0.001$) at Days 15 & 28 (Fig. 5).
- After 28 days of treatment with 12.5, 50 and 200 mg BID or placebo demonstrated highly statistically significant reductions at all doses ($p \leq 0.0014$) from baseline in CS-VAS of 24.7, 22.9, 26.5 and 8.3 mm, respectively (Fig. 5).
- CS-VAS shows clear separation from placebo as early as Day 15 at all doses (Fig. 5).

Conclusions

- Improvements in objective cough frequency observed with BLU-5937 also result in concomitant improvements in cough-related quality of life and perceived cough severity.
- SOOTHE was not powered to observe differences in patient-reported outcomes; significant changes over placebo were still observed at multiple timepoints in both CS-VAS and LCQ.
- SOOTHE demonstrated the potential of BLU-5937 to improve the patient-reported burden of RCC.

References

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