New data reinforces strength of once-daily COPD portfolio in improving lung function, shortness of breath and reducing rate of exacerbations

- *BLAZE study showed once-daily QVA149 significantly improved patient self-reported shortness of breath and lung function compared to placebo and tiotropium 18 mcg*[1]

- *SPARK results showed that QVA149 significantly reduced rate of all exacerbations compared to glycopyrronium 50 mcg and open-label tiotropium 18 mcg*[2,3]

- *Pooled GLOW 1 and 2 data showed once-daily Seebri® Breezhaler® (glycopyrronium) significantly improved lung function in the first 4 hours following morning administration compared to open-label tiotropium*[4]

Tokyo, Japan – 22 May 2013: Sosei Group Corporation ("Sosei"; TSE Mothers Index: 4565) highlights that further data from the once-daily chronic obstructive pulmonary disease (COPD) clinical trial programs were presented today by Novartis at the American Thoracic Society (ATS) International Conference (Philadelphia, USA). In total, Novartis presented 27 abstracts, featuring latest findings from the IGNITE clinical trial program including BLAZE[1] and SPARK[2,3,6,7] studies, plus data from pooled GLOW1 and 2 studies[4,8,9,10].

The BLAZE study showed that after six weeks of treatment, QVA149 significantly improved patient self-reported shortness of breath during daily activities versus both placebo ($p<0.001$) and tiotropium 18 mcg ($p=0.021$)[1]. BLAZE was the first study to evaluate direct electronic patient self-reported shortness of breath and showed that QVA149 significantly improved lung function versus placebo and tiotropium 18 mcg (as demonstrated by mean FEV_1) at all time points (45 minutes pre-dose to four hours post-dose) after six weeks of treatment ($p<0.001$)[1].

The SPARK study, recently published in Lancet Respiratory Medicine[14], demonstrated that QVA149 significantly reduced the rate of all COPD exacerbations (mild, moderate and severe) by 15% versus glycopyrronium 50 mcg ($p=0.0012$) and 14% versus OL tiotropium 18 mcg ($p=0.0017$)[2,3]. The primary endpoint of the study was also met since QVA149 demonstrated a significantly reduced rate of moderate or severe COPD exacerbations by 12% versus glycopyrronium ($p=0.038$)[2,3]. The rate of moderate or severe exacerbations was numerically lower ($p=0.096$) in patients on QVA149 compared to OL tiotropium 18 mcg[2,3]. SPARK also showed that patients receiving QVA149 had substantially improved lung function (measured by trough FEV_1) compared to glycopyrronium 50 mcg and OL tiotropium 18 mcg (both $p<0.0001$)[2,6]. In addition, QVA149 showed significant differences in health-related quality of life as demonstrated by St George's Respiratory Questionnaire (SGRQ) total scores of QVA149 versus glycopyrronium 50 mcg ($p<0.01$) and OL tiotropium 18 mcg ($p<0.05$)[2,6].

All treatments in the BLAZE and SPARK studies had an acceptable safety profile with no meaningful differences between the treatment groups in the incidence of adverse or serious adverse events[1,2,7].

In a pooled analysis of GLOW1 and GLOW2 data, once-daily glycopyrronium 50 mcg (Seebri® Breezhaler®) demonstrated significant improvements in lung function during first 4 hours following morning administration (measured by FEV_1 AUC_{0-4h}) versus placebo and OL tiotropium 18 mcg, at Day 1, 12 weeks and 26 weeks[4]. Once-daily glycopyrronium 50 mcg also demonstrated sustained improvements in lung function (measured by trough FEV_1) versus placebo over the long term[4]. Glycopyrronium 50 mcg was well-tolerated with a similar incidence of adverse events to placebo and OL tiotropium 18 mcg[9].

About the study designs

BLAZE was a 6-week, multicenter, blinded, double-dummy, placebo-controlled, 3-period crossover study[1]. Patients with moderate to severe COPD (N=247) were randomized to once-daily QVA149 (indacaterol maleate 110 mcg / glycopyrronium 50 mcg), tiotropium 18 mcg or placebo to assess the effect of QVA149 on patient self-reported shortness of breath[1].

SPARK was a 64-week, multicenter, double-blind, parallel-group, active controlled study assessing QVA149 (indacaterol maleate 110 mcg / glycopyrronium 50 mcg) versus glycopyrronium 50 mcg and OL tiotropium 18 mcg on the rate of moderate to severe COPD exacerbations in 2,224 patients with severe to very severe COPD[14].

GLOW1 and **GLOW2** were multicenter, randomized, double-blind, placebo-controlled, parallel group studies in patients with moderate to severe COPD[15,16]. GLOW1 was a 26 week study with 822 patients randomized to receive once-daily glycopyrronium 50 mcg (Seebri® Breezhaler®) or placebo[15]. GLOW2 was a 52 week study with 1,066 patients randomized to receive once-daily glycopyrronium 50 mcg or placebo, and included an exploratory arm to compare the effects of once-daily OL tiotropium 18 mcg versus placebo and glycopyrronium 50 mcg[16].

– Ends –

Enquiries

Sosei Group Corporation
Tokyo Office
Milica STOJKOVIC,
Investor Relations
+81-(0)3-5210-3399
mstojkovic@sosei.com

London Office
Kathryn LYDON, PA to CEO & Corporate Communication
+44-(0)20-7691-0983
klydon@sosei.com

Notes for editors

About Seebri® Breezhaler®:

Seebri® Breezhaler® (glycopyrronium bromide) is an effective and generally well-tolerated once-daily long-acting muscarinic antagonist (LAMA) indicated as maintenance therapy for the treatment of the symptoms of adult patients with chronic obstructive pulmonary disease (COPD)[18]. Glycopyrronium bromide was licensed to Novartis in April 2005 by Sosei and its co-development partner Vectura.

Phase III data from the GLOW 1, 2 and 3 studies demonstrated that glycopyrronium 50 mcg delivered rapid and significant sustained improvements in lung function (measured by mean FEV_1) post-morning dose on Day 1 compared with placebo and sustained this for 24 hours over 52 weeks, and significantly improved shortness of breath, heath related quality of life, exacerbations and exercise endurance versus placebo[15,16,19] and was generally safe and well tolerated.

About QVA149:
QVA149 is an investigational inhaled, once-daily, fixed-dose combination of indacaterol maleate and glycopyrronium bromide. QVA149 is being investigated for the maintenance treatment of COPD in the Phase III IGNITE clinical trial program. IGNITE is one of the largest international clinical trial programs in COPD comprising 10 studies in total (ILLUMINATE, SHINE, BRIGHT, ENLIGHTEN, SPARK, BLAZE, ARISE, BEACON, RADIATE, LANTERN) with more than 7,000 patients across 42 countries[14,17,20-30]. The first eight studies have already completed in 2012. The studies are designed to investigate efficacy, safety and tolerability, lung function, exercise endurance, exacerbations, shortness of breath and quality of life.

All Novartis inhaled COPD portfolio products are being developed for delivery via the Breezhaler® device, a single-dose dry powder inhaler (SDDPI)[18], which has low air flow resistance, making it suitable for patients with airflow limitation[31].The Breezhaler® device allows patients to hear, feel and see that they have taken the drug correctly[18].

About COPD
COPD is a progressive disease associated mainly with tobacco smoking, air pollution or occupational exposure, which can cause obstruction of airflow in the lungs resulting in debilitating bouts of breathlessness. It affects an estimated 210 million people worldwide[11] and is predicted to be the third leading cause of death by 2020[5]. Although COPD is often thought of as a disease of the elderly, 50% of patients are estimated to be within the ages of 50 and 65, which means that half of the COPD population are likely to be impacted at the peak of their earning power and family responsibilities[12].

About Sosei
Sosei is an international biopharmaceutical company anchored in Japan with a global reach. It practises a reduced risk business model by acquiring compounds from, and bringing compounds into, Japan through exploitation of its unique position within global markets.

For further information about Sosei, please visit www.sosei.com.

Forward-looking statements
This press release contains forward-looking statements, including statements about the discovery, development and commercialisation of products. Various risks may cause Sosei's actual results to differ materially from those expressed or implied by the forward-looking statements, including: adverse results in clinical development programmes; failure to obtain patent protection for inventions; commercial limitations imposed by patents owned or controlled by third parties; dependence upon strategic alliance partners to develop and commercialise products and services; difficulties or delays in obtaining regulatory approvals to market products and services resulting from development efforts; the requirement for substantial funding to conduct research and development and to expand commercialisation activities; and product initiatives by competitors. As a result of these factors, prospective investors are cautioned not to rely on any forward-looking statements. We disclaim any intention or obligation to update or revise any forward-looking statements, whether as a result of new information, future events or otherwise.

References

1. Mahler D *et al*. Superior lung function with once-daily QVA149 translates into improvements in patient reported breathlessness compared with placebo and tiotropium in COPD patients: the BLAZE study. [ATS abstract 45308; Session C20; Date: May 21, 2013 Time: 8:15-10:45].
2. Wedzicha W *et al*. Efficacy and safety of QVA149 versus glycopyrronium and tiotropium in severe to very severe COPD: the SPARK study. [ATS abstract 40727; Session B23; Date: May 20, 2013 Time: 8:15 -9:15].
3. Wedzicha W *et al*. Dual bronchodilation with QVA149 reduces COPD exacerbations: the SPARK study. [ATS abstract 40759; Session B23; Date: May 20, 2013 Time: 8:15 -9:15].
4. Roche N *et al*. Rapid bronchodilation with once-daily glycopyrronium: the importance of optimizing lung function in the morning. [ATS abstract 40403; Session C45; Date: May 21, 2013 Time: 10:45-12:30].

5. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease. Updated 2013. http://www.goldcopd.org/guidelines-global-strategy-for-diagnosis-management.html. Last accessed 2 May 2013.
6. Decramer M *et al*. Once-daily QVA149 improves health-related quality of life in patients with severe to very severe COPD: the SPARK study. [ATS abstract 40786; Session C45; Date: May 21, 2013 Time: 10:45-12:30].
7. Decramer M *et al*. Safety and tolerability of QVA149, glycopyrronium and tiotropium in patients with severe to very severe COPD: the SPARK study. [ATS abstract 41616; Session A43; Date: May 19, 2013 Time: 10:45-12:30].
8. D'Urzo A *et al*. Glycopyrronium once daily provides sustained bronchodilation and improves symptoms in various subgroups of patients with COPD. [ATS abstract 40505; Session C45; Date: May 21, 2013 Time: 10:45-12:30].
9. Kerwin E *et al.* Glycopyrronium is safe and well tolerated in patients with moderate-to-severe COPD. [ATS abstract 40518; Session C45; Date: May 21, 2013 Time: 10:45-12:30].
10. D'Urzo A *et al.* Glycopyrronium once daily improves patient-reported symptom scores in patients with COPD. [ATS abstract 40519; Session C45; Date: May 21, 2013 Time: 10:45-12:30].
11. Global Alliance Against Chronic Respiratory Diseases (GARD). Global surveillance, prevention and control of chronic respiratory diseases: a comprehensive approach. Available at: http://www.who.int/gard/publications/GARD%20Book%202007.pdf. Last accessed 2 May 2013.
12. Fletcher MJ *et al*. COPD Uncovered: An International survey on the impact of chronic obstructive pulmonary disease (COPD) on a working age population. *BMC Public Health* 2011;**11**:612.
13. daCosta M *et al.* The burden of chronic obstructive pulmonary disease among employed adults. *Int J Chron Obstruct Pulmon Dis* 2012;**7**:211-219. Published online 2012 March 19. doi: 10.2147/COPD.S29280. Last accessed 2 May 2013.
14. Wedzicha JA *et al*. Analysis of Chronic Obstructive Pulmonary Disease Exacerbations with the Dual Bronchodilator QVA149 Compared with Glycopyrronium and Tiotropium (SPARK): a Randomized, Double-blind, Parallel-group Study. *Lancet Respir Med* 2013 http://www.thelancet.com/journals/lanres/onlinefirst Last Accessed 2 May 2013
15. D'Urzo A *et al*. (2011). Efficacy and safety of once-daily NVA237 in patients with moderate-to-severe COPD: the GLOW1 trial. *Respiratory Research*.12:156.
16. Kerwin E *et al*. (2012). Efficacy and safety of NVA237 versus placebo and tiotropium in patients with COPD: The GLOW2 study. *Eur Resp J.* 40(5):1106-1114.
17. EMA, 2012. Onbrez® Breezhaler® (indacaterol) EU Summary of Product Characteristics. [Online] July 26, 2012 Available at: http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/001114/human_med_001219.jsp&mid=WC0b01ac058001d124. Last accessed 2 May 2013.
18. EMA. 2012. Seebri Breezhaler EU Summary of Product Characteristics. [Online] 17 October 2012. Available at: http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/002430/WC500133769.pdf. Last accessed 2 May 2013.
19. Beeh K *et al*. (2012). Once-daily NVA237 improves exercise endurance from first dose in patients with COPD: the GLOW3 trial. *Int J Chron Obstruct Pulmon Dis*.7:503-513.
20. Beeh *et al*. QVA149 once daily improves exercise tolerance and lung function in patients with COPD: the BRIGHT study. [BTS Winter Meeting 2012, Poster presentation P191; Date: 6 December; Time: 16:00-17:30].
21. Vogelmeier CF *et al*. Efficacy and safety of once-daily QVA149 compared with twice-daily salmeterol/fluticasone in patients with COPD (ILLUMINATE): a randomised, double-blind, parallel group study. *Lancet Respiratory Medicine*. 2013; 1 (1): 51-60
22. Bateman *et al*, 2012. Benefits of dual bronchodilation with QVA149 once daily versus placebo, indacaterol, NVA237 and tiotropium in patients with COPD: the SHINE study. Volume abstract 700179.
23. Dahl *et al*, 2012. QVA administered once daily provides significant improvements in lung function over 1 year in patients with COPD: The ENLIGHTEN study. Volume abstract 853405.
24. Novartis Pharma AG, data on file.*QVA149 A2322 (BLAZE).* s.l.:s.n.
25. Novartis Pharma AG, data on file.*QVA149 A1301 (ARISE).* s.l.:s.n.
26. ClinicalTrials.gov, n.d. Comparison of Safety and Efficacy of the Combination Product QVA149A Against the Concurrent Administration of the Individual Components, QAB149 and NVA237, in Patients With Chronic Obstructive Pulmonary Disease (COPD) (BEACON). [Online] Available at: www.clinicaltrials.gov/ct2/show/NCT01529632?term=BEACON&rank=6 [Accessed 2 May 2013].
27. Novartis Pharma AG, data on file. QVA149 A2339 (RADIATE).
28. ClinicalTrials.gov, n.d. A 26-week Treatment Randomized, Double-blind, Double Dummy, Parallel-group Study to Assess the Efficacy, Safety and Tolerability of QVA149 (Indacaterol / Glycopyrronium Bromide) Compared to Fluticasone/Salmeterol in Patients With Moderate to Severe Chronic Obstructive Pulmonary Disease. [Online]. Available at: www.clinicaltrials.gov/ct2/show/NCT01709903?id=01709903&rank=1 Last accessed 9 May 2013
29. FDA Access Data, n.d.*Spiriva Medical Review Part 2.* [Online] Available at: http://www.accessdata.fda.gov/drugsatfda_docs/nda/2004/21-395_Spiriva.cfm Last accessed 2 May 2013.
30. FDA Access Data, 2003.*Advair Medical Review.* [Online] Available at: www.accessdata.fda.gov/drugsatfda_docs/nda/2003/021077_S003_ADVAIR_DISKUS.pdf Last accessed 2 May 2013.
31. Pavkov *et al.* Characteristics of a capsule based dry powder inhaler for the delivery of indacaterol. *CMRO* 2010; 26; 11:2527–2533. doi:10.1185/03007995.2010.518916.