QVA149 Phase III study meets primary endpoint in reducing exacerbations in COPD patients and filings in EU and Japan by end of year

- *SPARK demonstrated QVA149 statistically significantly reduced rate of moderate-to-severe exacerbations compared to glycopyrronium 50 mcg*[1]

- *Study showed QVA149 statistically significantly reduced overall exacerbation rates compared to glycopyrronium 50 mcg and open-label tiotropium 18 mcg*[1]

- *SPARK is the final study of the IGNITE Phase III clinical trial program intended for initial regulatory filings*

Tokyo, Japan – 28 August 2012: Sosei Group Corporation ("Sosei"; TSE Mothers Index: 4565) confirms the information released today by Novartis that results from the fifth QVA149 (indacaterol maleate / glycopyrronium bromide) Phase III study, SPARK, met its primary endpoint of a reduced rate of moderate-to-severe COPD exacerbations compared to glycopyrronium bromide (Seebri® Breezhaler®)[1]. SPARK is the final study intended for initial regulatory filings of QVA149 in Europe and Japan, which are expected in Q4 2012. US filing of QVA149 is expected at the end of 2014. To date, the first five studies of the IGNITE QVA149 Phase III clinical trials program have all met their primary endpoints of efficacy, safety, exercise endurance, and reduction of exacerbations[1-5].

SPARK met its primary endpoint by demonstrating that patients treated with once-daily (QD) investigational QVA149 for 64 weeks demonstrated a clinically meaningful and statistically significant lower rate of moderate-to-severe COPD exacerbations compared to patients treated with QD glycopyrronium 50 mcg (p=0.038)[1]. The study also showed that the rate of moderate-to-severe exacerbations was numerically lower (p=0.096) in patients on QVA149 compared to open-label (OL) tiotropium 18 mcg[1].

A further analysis of the data demonstrated that QVA149 was statistically significantly more effective in reducing the overall rate of all exacerbations (mild, moderate and severe) compared to glycopyrronium 50 mcg (p=0.001) and OL tiotropium 18 mcg (p=0.002)[1]. The adverse event (AE) profile of QVA149 was similar to both glycopyrronium 50 mcg and OL tiotropium 18 mcg[1].

The management of COPD exacerbations is important to both patients and physicians, as exacerbations can impose a significant burden of morbidity, mortality, reduced quality of life and healthcare costs[6,7]. Frequent exacerbations are linked to an accelerated decline in lung function[8,9] and patients are also known to have a poorer quality of life[10]. Admissions to hospital due to exacerbations are increasing[11] and patients with more severe underlying disease account for around 70% of the direct medical costs of COPD[12].

SPARK was a 64-week, multi-center, randomized, double-blind, parallel-group, active controlled study designed to evaluate the effect of QVA149 (indacaterol maleate 110 mcg / glycopyrronium 50 mcg) QD versus glycopyrronium 50 mcg and QD OL tiotropium 18 mcg on moderate-to-severe COPD exacerbations in 2,224 patients with severe to very severe COPD[1].

QVA149 is an investigational inhaled, once-daily, fixed-dose combination of the long-acting beta$_2$-adrenergic agonist (LABA) indacaterol maleate, and the investigational long-acting muscarinic antagonist (LAMA) glycopyrronium bromide, being investigated for the 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 with more than 7,000 patients across 42 countries[1-5,13-20]. The first five studies (ILLUMINATE, SHINE, BRIGHT, ENLIGHTEN, SPARK) have already completed in 2012 with three additional studies (BLAZE, ARISE, BEACON) expected to complete by the end of the year. The

studies are designed to investigate efficacy, safety and tolerability, exercise endurance, exacerbations, breathlessness and quality of life[1-5,13-17].

CEO of Sosei, Shinichi Tamura commented:

"The SPARK study demonstrated a meaningful reduction in exacerbations in COPD patients; something that is of major benefit for patients and doctors and eases the burden of healthcare costs. We look forward to more detailed data from both glycopyrronium bromide (NVA237) and QVA149 at the upcoming European Respiratory Society meeting in Vienna in early September with the first filings for QVA149 expected in Europe and Japan by the end of this year."

– Ends –

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Notes for editors

About NVA237/QVA149

NVA237 (glycopyrronium bromide - Seebri® Breezhaler®) was licensed to Novartis in April 2005 by Sosei and its co-development partner, Vectura. It is an investigational LAMA developed as a once-daily inhaled maintenance therapy for the treatment of COPD. Phase III data from the GLOW1, 2 and 3 studies demonstrated that glycopyrronium bromide increased patients' lung function over a 24-hour period compared to placebo with a fast onset of action at first dose, and improved exercise endurance versus placebo[21-23].

QVA149 is an investigational inhaled, once-daily, fixed-dose combination of NVA237 and the LABA, indacaterol maleate, for which Novartis received European regulatory approval as Onbrez® Breezhaler® in November 2009. It was first launched in the EU in 150 mcg and 300 mcg once-daily doses. Most recently, Novartis launched the 75 mcg once-daily dose in the US under the brand name Arcapta™ Neohaler™. It is also available as a 150 mcg once-daily dose in Japan under the brand name Onbrez® Inhalation Capsules.

All of the Novartis COPD portfolio products are being developed for delivery via the Breezhaler® device, a single-dose dry powder inhaler (SDDPI), which has low air flow resistance, making it particularly suitable for patients with airflow limitation, such as COPD patients. 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[24] and is predicted to be the third leading cause of death by 2020[25]. 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[26].

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. ClinicalTrials.gov. Effect of QVA149 Versus NVA237 and Tiotropium on Chronic Obstructive Pulmonary Disorder (COPD) Exacerbations (SPARK). NCT01120691. http://www.clinicaltrials.gov/ct2/show/NCT01120691?term=NCT01120691.&rank=1. Last accessed 21 August 2012.
2. ClinicalTrials.gov. QVA149 versus Fluticasone/Salmeterol in Patients With Chronic Obstructive Pulmonary Disease (COPD) (ILLUMINATE). NCT01315249 http://www.clinicaltrials.gov/ct2/show/NCT01315249?term=NCT01315249&rank=1. Last accessed 21 August 2012.
3. ClinicalTrials.gov. A Study to Assess the Efficacy, Safety and Tolerability of Once-daily QVA149 in Patients With Moderate to Severe Chronic Obstructive Pulmonary Disease (COPD) (SHINE). NCT01202188. http://www.clinicaltrials.gov/ct2/show/NCT01202188?term=NCT01202188&rank=1. Last accessed 21 August 2012.
4. ClinicalTrials.gov. Effect of QVA149 on Exercise Tolerance in Patients With Chronic Obstructive Pulmonary Disease (COPD) (BRIGHT). NCT01294787. http://www.clinicaltrials.gov/ct2/show/NCT01294787?term=NCT01294787.&rank=1. Last accessed 21 August 2012.
5. ClinicalTrials.gov. A Study to Assess the Long-term Safety of QVA149 (ENLIGHTEN). NCT01120717. http://www.clinicaltrials.gov/ct2/show/NCT01120717?term=NCT01120717&rank=1. Last accessed 21 August 2012.
6. Simoens S *et al.* Clinical and economic analysis of antimicrobial therapy of chronic obstructive pulmonary disease exacerbations. *Int J Clin Pract.* 2007;**61**:200-206.
7. Hurst J et al. Chronic obstructive pulmonary disease: the clinical management of an acute exacerbation. Postgrad Med J. 2004;**80**:497-505.
8. Kanner R, *et al.* Lower respiratory illness promote FEV_1 decline in current smokers but not ex-smokers with mild chronic obstructive pulmonary disease. Results from the Lung Health Study. *Am J Respir Crit Care Med* 2001;**164**:358-64.
9. Donaldson G *et al.* Relationship between exacerbation frequency and lung function decline in chronic obstructive pulmonary disease. *Thorax.* 2002;**57**:847-52.
10. Seemungal TAR *et al.* Effect of exacerbation on quality of life in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med.* 1998;**157**:1418-22.
11. Lung and Asthma Information Agency. Trends in hospital admissions for lung disease. Fact sheet 2001/4. London: St George's Hospital Medical School.
12. Sullivan S *et al.* The economic burden of COPD. Chest. 200;117(suppl):5S-9S.
13. ClinicalTrials.gov. The Effect of QVA149 on Dyspnea in Patients With Chronic Obstructive Pulmonary Disease (COPD) (BLAZE). NCT01490125. http://www.clinicaltrials.gov/ct2/show/NCT01490125?term=NCT01490125.&rank=1. Last accessed 21 August 2012.
14. ClinicalTrials.gov. Long Term Safety and Tolerability of QVA149 Versus Tiotropium in Japanese Patients With Chronic Obstructive Pulmonary Disease (COPD) (ARISE). NCT01285492. http://www.clinicaltrials.gov/ct2/show/NCT01285492?term=NCT01285492.&rank=1. Last accessed 21 August 2012.
15. ClinicalTrials.gov. 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). http://www.clinicaltrials.gov/ct2/show/NCT01529632?term=BEACON&rank=6. Last accessed 22 August 2012.

16. ClinicalTrials.gov. Comparison of Long-term Safety of the Combination Product QVA149A Against Placebo and Standard of Care Treatment in Chronic Obstructive Pulmonary Disease Patients With Moderate to Severe Airflow Limitation (GLISTEN). http://www.clinicaltrials.gov/ct2/show/NCT01610037?term=GLISTEN&rank=1. Last accessed 22 August 2012.
17. ClinicalTrials.gov. The Effect of QVA149 on Health Related Quality of Life in Patients With Chronic Obstructive Pulmonary Disease (COPD) (QUANTIFY). http://clinicaltrials.gov/ct2/show/NCT01574651?term=QUANTIFY&rank=1. Last accessed 22 August 2012.
18. Onbrez® Breezhaler® (indacaterol) EU Summary of Product Characteristics May 31, 2011 http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/001114/human_med_001219.jsp&mid=WC0b01ac058001d124. Last accessed 21 August 2012.
19. FDA Access Data. Spiriva® HandiHaler® Medical Review Part 2, pages 37-38. http://www.accessdata.fda.gov/drugsatfda_docs/nda/2004/21-395_Spiriva.cfm. Last accessed 21 August 2012.
20. FDA Access Data. Advair Medical Review Nov. 17, 2003, Page 133. http://www.accessdata.fda.gov/drugsatfda_docs/nda/2003/021077_S003_ADVAIR_DISKUS.pdf. Last accessed 21 August 2012.
21. D'Urzo A, *et al*. Efficacy and safety of once-daily NVA237 in patients with moderate-to-severe COPD: the GLOW1 trial. *Respiratory Research* 2011;**12**:156 (7 December 2011).
22. Kerwin E, *et al*. Efficacy and safety of NVA237 versus placebo and tiotropium in patients with moderate-to-severe COPD over 52 weeks: The GLOW2 study. *Eur Resp J*. 2012. Published on July 26, 2012 (doi:10.1183/09031936.00040712). Last accessed 21 August 2012.
23. Beeh K, Drollmann A, Di Scala L, Smith R. Once-daily NVA237 improves exercise endurance from first dose in patients with COPD: the GLOW3 trial. *Int J Chron Obstruct Pulmon Dis*. 2012;7:503-513.
24. 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 21 August 2012.
25. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease. Updated 2011. http://www.goldcopd.org/guidelines-global-strategy-for-diagnosis-management.html. Last accessed 21 August 2012.
26. 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.