



## **Synta and Roche Form Discovery, Development, and Commercialization Alliance in Inflammation**

January 7, 2009

**\$25 Million in Upfront Committed Payments**

### **New Category of Oral Agents for the Potential Treatment of Rheumatoid Arthritis and Other Inflammatory Diseases**

LEXINGTON, Mass., Jan 07, 2009 (BUSINESS WIRE) -- Synta Pharmaceuticals Corp. (NASDAQ: SNTA) and Roche (SWX: ROG) announced today the formation of a strategic alliance to discover, develop, and commercialize small-molecule drugs targeting a novel family of ion channels that are critical to immune cell function, known as calcium release-activated calcium modulator (CRACM) channels. In preclinical models, the CRACM inhibitors discovered by Synta potently and selectively inhibit the secretion of pro-inflammatory factors such as TNF-alpha and IL-2, with minimal effects on other cells or signaling pathways. This program represents a new category of oral, targeted, disease-modifying agents for treating rheumatoid arthritis and a broad range of other inflammatory diseases.

Under the terms of the agreement, Roche will fund research to be conducted by Synta during an initial two-year research period. Roche will receive worldwide rights to develop and commercialize certain products identified prior to the end of this research period. Synta retains certain co-development and co-promotion rights. All preclinical, clinical, and commercial costs will be paid by Roche.

Synta will receive \$25 million in upfront cash license fees and committed research support, of which \$9 million will be provided in the form of research support over the initial research period. Synta will also be eligible to receive additional payments, for each of three licensed products, should specified development and commercialization milestones be successfully achieved. Development milestones across multiple indications of up to \$245 million could be earned for the first product, and up to half of this amount could be earned for each of the second and third products. Commercialization milestones of up to \$170 million could be earned for each of three products. Synta will receive tiered royalties on sales of all approved, marketed products.

"This agreement underscores both the potential of our novel ion channel inhibitors and the ability of the Synta drug discovery platform to generate high-quality, first-in-class drug candidates," said Safi Bahcall, Ph.D., President and Chief Executive Officer, Synta. "We believe that combining our leadership in the CRACM inhibitor field with Roche's expertise in inflammatory diseases will enable us to accelerate the development of an exciting new therapeutic category for patients."

"Synta has the most advanced programme in the field, with its lead candidate and other promising drug candidates soon progressing into the clinic," said Satwant Narula, Roche's Head of Discovery for Inflammation. "The CRACM channel inhibitor approach has tremendous potential to treat

rheumatoid arthritis and a wide range of other inflammatory diseases that have a high unmet need for oral, targeted, disease-modifying agents. Roche and Synta will work closely together to bring these potential therapies to patients."

"The Synta CRACM inhibitor program generated substantial interest among many leading global pharmaceutical companies. We believe this interest reflects the growing scientific excitement around the CRACM target; the size of the opportunity presented by a new category of disease-modifying agents for inflammation; and the strength of the Synta intellectual property portfolio and drug discovery capabilities," added Albert Hsia, Ph.D., Senior Director, Business Development, Synta. "We are enthusiastic about working with Roche in an alliance that combines the strengths of our two companies within a collaborative framework for rapid development of these promising CRACM inhibitor compounds."

### About Ion Channel Therapeutics

Ion channels, the gateways in cell membranes that regulate the flow of ions into and out of cells, play important roles in cell signaling. Certain ion channels allow electrically excitable cells, such as neurons or muscle cells, to discharge. Drugs that modulate these ion channels have proven to be a successful therapeutic category, with dozens of such drugs on the market and commonly prescribed for the treatment of various neurological and cardiovascular disorders.

The Synta research program targets an ion channel known as the CRACM channel, which is believed to play a key role specifically in immune cells rather than in neurons or muscle cells. CRACM channels regulate the calcium signaling pathway driving immune cell activation and secretion of TNF-alpha, IL-2, and other inflammatory factors. The therapeutic importance of inhibiting this calcium signaling pathway has been demonstrated through clinical experience with calcineurin inhibitors, such as cyclosporine, which are potent immunomodulators but have significant toxicities due to the broad role calcineurin plays in non-immune cells. In contrast to calcineurin, CRACM channels are believed to be critical exclusively to immune cell function. CRACM inhibitors therefore have the potential to achieve potent anti-inflammatory activity with an improved safety profile, creating a new category of disease-modifying agents comparable to biologic agents, such as TNF-alpha inhibitors, but orally available.

The Synta CRACM channel inhibitors have shown strong anti-inflammatory activity in preclinical studies both in vitro and in vivo, inhibiting T cell and mast cell activity, including cytokine release, degranulation, and immune cell proliferation. Potential applications include a wide range of inflammatory diseases and disorders for which modulating T cell and mast cell function has been shown to be critical, including rheumatoid arthritis, asthma, chronic obstructive pulmonary disease (COPD), allergy, transplant rejection, and other autoimmune diseases and inflammatory conditions.

### CRACM Channel References

Vig, M., and Kinet, J.P. Calcium signaling in immune cells. *Nat. Immunol.* 10, 21-7 (2009).

Feske, S., Prakriya, M., Rao, A., and Lewis, R.S. A severe defect in CRAC Ca<sup>2+</sup> channel activation and altered K<sup>+</sup> channel gating in T cells from immunodeficient patients. *J. Exp. Med.* 202, 651-62 (2005).

Lewis, R.S. Calcium signaling mechanisms in T lymphocytes. *Annu. Rev. Immunol.* 19, 497-521

(2001).

Cahalan, M.D., and Chandy, K.G. Ion channels in the immune system as targets for immunosuppression. *Curr. Opin. Biotechnol.* 8, 749-56 (1997).

Hoth, M., and Penner, R. Depletion of intracellular calcium stores activates a calcium current in mast cells. *Nature.* 355, 353-6 (1992).

#### About Synta Pharmaceuticals

Synta Pharmaceuticals Corp. is a biopharmaceutical company focused on discovering, developing, and commercializing small-molecule drugs to extend and enhance the lives of patients with severe medical conditions, including cancer and chronic inflammatory diseases. Synta has a unique chemical compound library, an integrated discovery engine, and a diverse pipeline of clinical- and preclinical-stage drug candidates with distinct mechanisms of action and novel chemical structures. All Synta drug candidates were invented by Synta scientists using our compound library and discovery capabilities. For more information, please visit [www.syntapharma.com](http://www.syntapharma.com).

#### About Roche

Headquartered in Basel, Switzerland, Roche is one of the world's leading research-focused healthcare groups in the fields of pharmaceuticals and diagnostics. As the world's biggest biotech company and an innovator of products and services for the early detection, prevention, diagnosis and treatment of diseases, the Group contributes on a broad range of fronts to improving people's health and quality of life. Roche is the world leader in in-vitro diagnostics and drugs for cancer and transplantation, and is a market leader in virology. It is also active in other major therapeutic areas such as autoimmune diseases, inflammatory and metabolic disorders and diseases of the central nervous system. In 2007 sales by the Pharmaceuticals Division totaled 36.8 billion Swiss francs, and the Diagnostics Division posted sales of 9.3 billion francs. Roche has R&D agreements and strategic alliances with numerous partners, including majority ownership interests in Genentech and Chugai, and invested over 8 billion Swiss francs in R&D in 2007. Worldwide, the Group employs about 80,000 people. Additional information is available on the Internet at [www.roche.com](http://www.roche.com).

#### Safe Harbor Statement

This media release may contain forward-looking statements about either company. Such forward-looking statements can be identified by the use of forward-looking terminology such as "will", "would", "should", "expects", "anticipates", "intends", "plans", "believes", "may", "estimates", "predicts", "projects", or similar expressions intended to identify forward-looking statements. Such statements, including statements relating to the timing and progress of our clinical and preclinical programs, reflect our current views with respect to future events and are based on assumptions and subject to risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such forward-looking statements, including those described in documents filed with the Securities and Exchange Commission. Neither company undertakes an obligation to publicly update forward-looking statements, whether because of new information, future events or otherwise, except as required by law.

SOURCE: Synta Pharmaceuticals Corp.

Synta Contacts:

Synta Pharmaceuticals Corp.  
Rob Kloppenburg, 781-541-7125

or

MacDougall Biomedical Communications  
Doug MacDougall, 781-235-3060

or

Roche Contacts:

Roche Pharma Partnering  
Peter Sandbach, +41 61 688 3408  
peter.sandbach@roche.com

or

Roche Public Affairs  
Darren E. Wilson, 973-562-2232  
darren\_e.wilson@roche.com