Synta Announces Launch of Proprietary Small Molecule Hsp90-inhibitor Drug Conjugate Platform

September 10, 2013

– Novel drug conjugates that exploit Hsp90 biology to selectively deliver potent anti-cancer payloads to cancer cells –

– Over 350 HD-Conjugates developed, including HD-Conjugated Alimta®, Nexavar®, Paraplatin®, Revlimid®, Sutent®, Taxotere®, Velcade®, Zytiga® –

– Broad intellectual property platform; first IND expected in next 18 months –

– Company to host conference call and webcast today at 5:00 PM EDT –

LEXINGTON, Mass.--(BUSINESS WIRE)--Sep. 10, 2013-- Synta Pharmaceuticals Corp. (NASDAQ: SNTA) today announced the launch of its Hsp90-inhibitor Drug Conjugate (HDC) platform, which leverages the Company's expertise in chaperone biology and medicinal chemistry to create a new class of anti-cancer therapies.

The need: delivering potent anti-cancer drugs directly to tumors

Current oncology therapeutics generally fall into two categories: cytotoxic agents and molecularly targeted therapies. Cytotoxic agents are often broadly active, but have the disadvantage of high toxicity caused by damage to normal cells, which limits their utility. Drugs that target specific protein drivers of cancer cell growth are generally more tumor selective, yet often lead to tumor resistance via point mutations in their target (e.g. ALK, BRAF, EGFR inhibitors) or activation of alternative signaling pathways (e.g., MEK, ERK, or AKT upregulation).

Targeted delivery strategies, such as Antibody Drug Conjugates (ADCs), offer a solution to these limitations by delivering potent anti-cancer payloads more directly to tumors. HDCs offer many of the advantages of antibody-driven targeted delivery with potentially broader applicability. Because of its unique properties, Hsp90 (heat shock protein 90) may represent one of the most compelling targets for delivering drug payloads to tumors.

HDCs exploit the preferential accumulation of Hsp90-inhibitors in tumors to increase the selective delivery of anti-cancer payloads

Hsp90 is a chaperone protein required by many cancer cells to maintain the stability and function of numerous proteins that drive cancer cell growth, survival, and metastasis. Small molecule inhibitors of Hsp90, including Synta's drug candidate ganetespib as well as first-generation inhibitors such as 17-AAG and its derivatives, are retained in tumors for as much as 20 times longer than in blood or normal tissue [1, 2]. These properties are believed to be due to overexpression of an active form of Hsp90 in cancer cells as compared to normal tissues, and have been recently applied for tumor

imaging [3, 4].

HDCs are drugs consisting of an Hsp90 inhibitor (targeting moiety) joined to an anti-cancer agent (payload) via a cleavable chemical linker optimized for controlled release of payload drug inside cancer cells. Because HDCs are small molecules, they diffuse into the cell passively, avoiding reliance on cell surface antigens or transporters.

Essentially, the active Hsp90 in tumors acts as a magnet to attract the Hsp90-inhibitor moieties in HDCs, bringing the entire HDC molecule preferentially to tumors. This results in higher concentration and longer duration of active payload drug inside cancer cells than occurs with standard administration of unconjugated chemotherapy or other payloads. The enhanced delivery creates the potential for greater cancer cell killing and reduced side effects.

The Synta HDC platform and intellectual property: Over 350 HD-Conjugates developed to date

Synta has developed over 350 HD-Conjugated chemotherapeutics, kinase inhibitors, hormone therapies, immunomodulators, and epigenetic modifiers, creating the potential for next-generation compounds in each of these categories.

Proof-of-concept has been demonstrated in preclinical models of cancer, showing both improved delivery, including greatly increased concentration and duration of payload in tumors as compared to plasma and normal tissues, as well as significantly improved anti-tumor activity compared to administration of unconjugated payload.

HDCs are a promising new therapeutic class with the potential to enhance the safety and efficacy of a wide range of small molecule anti-cancer drugs. The portfolio of HDCs developed by Synta to date, using a broad range of Hsp90-inhibitor moieties, cleavable linkers, and anti-cancer payloads, includes:

Category	Example synthesized HDCs
Alkylating agents	HD-Conjugated bendamustine (Treanda®) HD-Conjugated temozolomide (Temodar®)
Anthracyclines	HD-Conjugated doxorubicin (Adriamycin®)
Antimetabolites	HD-Conjugated 5-FU (Xeloda®) HD-Conjugated pemetrexed (Alimta®)
Camptothecins	HD-Conjugated SN-38 (Camptosar®) HD-Conjugated topotecan (Hycamtin®)
Epigenetic modifiers	HD-Conjugated vorinostat / SAHA (Zolinza®) HD-Conjugated panobinostat (Faridak®)
Hormonal therapy	HD-Conjugated fulvestrant (Faslodex®) HD-Conjugated abiraterone (Zytiga®)
IMIDs	HD-Conjugated lenalidomide (Revlimid®) HD-Conjugated pomalidomide (Pomalyst®)
Microtubule stabilizers	HD-Conjugated docetaxel (Taxotere®)
Platinums	HD-Conjugated carboplatin (Paraplatin®)
Proteasome inhibitors	HD-Conjugated bortezomib (Velcade®)

Tyrosine Kinase Inhibitors	HD-Conjugated sunitinib (Sutent®) HD-Conjugated sorafenib (Nexavar®)

Broad intellectual property

Synta has filed worldwide patent applications that include comprehensive claims covering the HDC platform, compositions of matter for the over 350 compounds noted above, methods for identifying therapeutically effective compounds and methods of use of such compounds against a wide range of diseases and conditions. Publication of the first patent filings is expected within the next several weeks.

HDCs compared to other targeted delivery strategies

HDCs rely on the presence of active Hsp90 in tumors – which may lead to broader application than ADCs, whose development has focused on cancers uniquely expressing a surface antigen that can be targeted with an antibody (e.g., HER2+ breast cancer) [5]. Another advantage of HDCs is that they can achieve substantially higher payload concentrations inside cancer cells than may be achieved with ADCs, due to differences in uptake mechanism (passive diffusion vs. active uptake). HDCs can therefore deliver a much broader range of payloads as compared to ADCs.

Partnering

The Synta HDC platform offers multiple partnering opportunities centered on improved delivery of both approved and investigational anti-cancer agents, across a broad range of oncology indications. Synta intends to realize the breadth of application of this platform through a series of focused pharmaceutical company partnerships.

HDC platform upcoming milestones

Synta expects the first patent filings covering the HDC platform to be published in the next several weeks. The company anticipates a number of scientific presentations and publications highlighting the potential of HDCs in 2014, and expects one or more IND filings within the next 18 months.

“From the idea, to proof-of-concept and the creation of a broad platform with strong intellectual property protection, our scientists have made tremendous progress in creating an exciting, new class of anti-cancer therapies,” said Safi R. Bahcall, Ph.D., President and CEO. “We are hopeful this platform can lead to meaningful improvements over existing therapies, and ultimately to better outcomes for patients.”

For further information on the Synta HDC platform, please click here.

Company to host conference call and webcast today, September 10, at 5:00 PM EDT

Management will conduct a conference call at 5:00 p.m. (EDT) today to discuss the launch of the new HDC drug technology platform. The conference call will be webcast live and can be accessed by logging on to the Investors section of the Synta Pharmaceuticals website, www.syntapharma.com.

Participants can also connect by phone by dialing (877) 407-8035 or (201) 689-8035 prior to the start of the call. A replay will be available from 8:00 p.m. (EDT) this evening through midnight (EDT) on September 17. To access the replay, dial (877) 660-6853 or (201) 612-7415 and refer to conference ID 420728.

References

1. J.L. Eiseman et al. Cancer Chemother Pharmacol. 2005 Jan;55(1):21-32
2. K.P. Foley et al. AACR-NCI-EORTC Conference 2009 (abstr #C91)
3. G. Chiosis, L. Neckers, ACS chemical biology. 2006;1(5):279-284
4. J. F. Gerecitano et al., J Clin Oncol 31, 2013 (suppl; abstr 11076)
5. B. A. Teicher and R. V. J. Chari, Clin Canc Res 2011; 17: 6389-6397

About Ganetespib

Ganetespib, an investigational drug candidate, is a selective inhibitor of heat shock protein 90 (Hsp90), a molecular chaperone which controls the folding and activation of a number of client proteins that drive tumor development and progression. Many solid and hematologic tumors are dependent on Hsp90 client proteins including proteins involved in “oncogene addiction” (ALK, HER2, mutant BRAF and EGFR, androgen receptor, estrogen receptor, JAK2); proteins involved in resistance to chemotherapy and radiation therapy (ATR, BCL2, BRCA1/2, CDK1/4, CHK1, survivin, and WEE1); proteins involved in angiogenesis (HIF-1alpha, VEGFR, PDFGR, and VEGF); and proteins involved in metastasis (MET, RAF, AKT, MMPs, HIF-1alpha, and IGF-1R). In preclinical models, inhibition of Hsp90 by ganetespib results in the inactivation, destabilization, and eventual degradation of these cancer-promoting proteins. Ganetespib is being evaluated in trials in lung cancer, breast cancer, and other tumor types. The most common adverse event seen to date has been transient, mild or moderate diarrhea, which has been manageable with standard supportive care. Information on these trials can be found at www.clinicaltrials.gov.

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.

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This media release may contain forward-looking statements about Synta Pharmaceuticals Corp. 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 of patent publications, scientific publications and presentations covering the HDC platform, the plans relating to HDC partnerships, and the timing of IND filings for HDC drug candidates, 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 "Risk Factors" of our Form 10-K for the year ended December 31, 2012 as filed with the Securities and Exchange Commission. Synta undertakes no obligation to publicly update forward-looking statements, whether because of new information, future events or otherwise, except as required by law.

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