Nantcell announces new Celgene Investment

January 4, 2019

Immunotherapy Company Will Present Findings at the JP Morgan Healthcare Conference in San Francisco on January 7th

Second Round Crossover Funding Brings Celgene's Investment to $105M in NantCell Valued at $4 Billion

Currently Enrolling Patients in Advanced Stage Trials in 15 Indications for Registration Intent

Deep Pipeline Of 28 Unique Molecules With 14 First in Human Studies in Over 1,000 Patients to Date

Los Angeles, CA, January 4, 2019 - NantCell and it's founder Dr. Patrick Soon-Shiong announced today that Celgene has completed its crossover investment in NantCell. Dr. Soon-Shiong will be introducing the company at the 37th Annual JP Morgan Healthcare Conference at the Westin St. Francis Hotel, San Francisco on Monday, January 7th at 8:30am.

NantCell is a privately held immunotherapy company, whose goal is to employ a broad portfolio of biological molecules that will enable it to develop a cancer vaccine to combat multiple tumor types without the use of high-dose chemotherapy. NantCell has one of the most comprehensive late stage clinical pipelines of an integrated platform of immunotherapy technologies addressing both the innate (activated macrophage and natural killer cell) and the adaptive immune system (dendritic, CD4 and CD8 killer T cells). Currently the company is actively enrolling patients for registration trials in 15 indications.

On December 19, 2018, Celgene completed a crossover funding round of $30 million in NantCell at a $4 billion valuation, bringing its overall investment in the company to $105 million with a 2.8% ownership in the company. This follows the May 2015 Celgene initial investment of $75 million in NantCell.

"We have partnered with Dr. Soon-Shiong and his mission to change the course of cancer from the very beginning," said Mark Alles, Chairman and CEO of Celgene. "From his invention of Abraxane, to acquiring his company in 2010, to launching this protein nanoparticle drug as the backbone of immunotherapy to its current blockbuster status, and now to supporting his vision at NantCell of developing a chemo free cancer vaccine utilizing the body's own immune system. Celgene invested in NantCell since its inception in 2015 and we are excited to extend this partnership today with the significant clinical progress he has made in developing cytokines and bispecific proteins in the ongoing quest to conquer this disease," said Alles. Celgene announced on January 3, 2019 that it would be acquired by Bristol-Myers Squibb for $74 billion.

"To our knowledge" said Soon-Shiong, "there is no other biotech or large pharma company with NantCell's broad pipeline of bispecific and trispecific fusion cytokine proteins, peptides, mRNA, monoclonal antibodies, neoepitope and tumor associated vaccine delivery and cell therapy products, all in clinical phase of development, across multiple indications, for the treatment of cancer and infectious disease. We are very pleased with Celgene's continued investment in the company and our shared vision of developing a chemotherapy free cancer vaccine."

"With the clinical advances of the technology platforms across multiple tumor types at NantCell, the company is now poised to integrate the technologies developed at the two early stage immunotherapy public companies, NantHealth and NantKwest," said Dr. Soon-Shiong, founder of all three companies. "The adenovirus and yeast vector delivery systems in NantCell compliments the tumor associated antigen and neoepitope discovery engine (GPS CancerTM) developed by NantHealth, enabling the subcutaneous delivery of the neoepitopes to enable the recruitment of T cells that target only expressed cancer mutations. The bispecific fusion cytokine proteins of NantCell stimulates the patient's autologous primary NK and T cells, thereby supplementing the off-the-shelf, cryopreserved haNK cells developed by NantKwest. Collectively the immunotherapy platforms in NantCell, NantHealth and NantKwest serve as a comprehensive path to the development of a cancer vaccine," said Soon-Shiong.

Preclinical Pipeline, Technology Platforms and IND Pipeline:
Specifically, NantCell has 28 unique molecules in its preclinical pipeline consisting of fusion proteins, mRNA, cytokines and monoclonal antibodies including checkpoints and novel cytokine fusion proteins, six of which are IND ready with anticipated filings in 2019. The company has developed a novel proprietary library of fully human single chain variable fragment antibodies (ScFv) with a diversity greater than 1012. This library has yielded fully human monoclonal antibodies with high affinity target binding and is being incorporated into chimeric antigen receptor (CAR) in both off-the-shelf NK cell lines as well as autologous primary NK and T cells for the development of novel cell therapy products. To enable intracellular uptake of both DNA and mRNA, NantCell has also developed novel methods of scalable electroporation enabling high viability and high expression of the desired genes in NK92 cell line, and in primary NK and T cells. In addition, NantCell has developed an automated method of a fully closed system for manufacturing targeted NK cell lines, primary NK and T cells (GMP in the box).

Current Phase 1 and Phase 2 Development Program:
In addition to the preclinical pipeline above, currently the company's activated clinical programs include seven (7) molecules in Phase 1, four (4) molecules in Phase 2, and three (3) molecules in registration clinical trials, across multiple indications. The deep clinical pipeline of 14 unique biomolecules have been tested in over 1,000 patients to date, to evaluate the safety and initial efficacy profiles of these novel molecules as **first in human single agent** studies.

In 2017 and 2018, the company initiated **combination** studies of these individual molecules and over 20 Investigational New Drugs (INDs) were authorized by the FDA to enable Phase 1 safety studies using these fusion proteins, monoclonal antibodies, tumor associated adenoviral and yeast delivery systems to evaluate safety and early efficacy of these combinations, termed **QUILT** Trials . Phase 1 safety and efficacy clinical data for this **cancer vaccine** of the combined molecules has been completed for multiple tumor types, including metastatic pancreatic cancer, triple negative breast cancer, head and neck cancer, lung cancer and bladder cancer. Preliminary data was presented at the SITC conference in November 2018.

Registration Trials with NantCell's Lead Cytokine Fusion Protein:
NantCell has initiated registration trials of its lead cytokine fusion protein in 15 indications. The lead IL15/Fc bispecific fusion protein and cytokine has entered into two registration trials in bladder cancer and obtained **Fast Track Designation** for the treatment of relapsed non-muscle invasive bladder cancer. The company anticipates completion of accrual in 2019 with a read out of efficacy data by the third quarter.

NantCell has also began enrollment in single arm pivotal trials of this bispecific IL15/Fc cytokine in 12 distinct cancer indications, in which patients have failed checkpoint inhibitors. These single arm pivotal trials include patients in the following indications; non-small cell lung cancer (NSCLC), small cell lung cancer (SCLC), urothelial carcinoma, head and neck squamous cell carcinoma (HNSCC), Merkel cell carcinoma (MCC), melanoma, renal cell carcinoma (RCC), gastric cancer, cervical cancer, hepatocellular carcinoma (HCC), microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) solid tumor cancer and colorectal cancer (CRC).

In addition, the company began enrollment in a pivotal randomized trial of patients with non- small cell lung cancer comparing checkpoint therapy alone versus checkpoint therapy in combination with the IL15/Fc fusion protein as a chemotherapy free first line therapy in lung cancer.

Registration Trials at NCI: Two molecules are actively being studied in Phase 3 trials at the NCI for the treatment of patients with Ewing's sarcoma and Recurrent Chordoma.

Registration Trial in Collaboration with NantKwest: The bispecific IL15/Fc cytokine in combination with NantKwest's high affinity NK cell (haNK) and a checkpoint inhibitor has been authorized to begin enrollment in patients with relapsed Merkel cell carcinoma.

GMP Manufacturing:
The company has developed and completed GMP manufacturing facilities for its lead bispecific cytokine IL15/Fc fusion protein, for its adenovirus and yeast delivery systems and novel "GMP in a Box" automated manufacturing for its targeted natural killer and T cell therapies.

About the Concept of Chemotherapy Free Cancer Vaccine:

The concept of activating the body's own immune system evolved during Dr. Soon-Shiong's studies on developing a micro encapsulated islet cell transplant in the 1990's. In 1993 he performed the world's first micro encapsulated islet transplant in a diabetic patient and published a paper entitled *"Prevention of CTL and NK Cell-Mediated Cytotoxicity by Microencapsulation," (Hormone and Metabolic Research, 1990, PG. 215-219)* demonstrating that the body's natural killer (NK) cells were responsible for attacking foreign implanted tissue. Inspired by the thought that the cancer cell had discovered a means to trick the body and induce tolerance, Dr. Soon-Shiong began the concept of inventing a nanoparticle to breach the tumor micro environment to activate the innate immune system. By 1998, he invented the first albumin-bound nanoparticle, Abraxane, harnessing the protein pathways (GP60) to enter the tumor micro environment and activate macrophages to attack cancer cells. Abraxane was approved in 2005 and acquired by Celgene in 2010. The drug has since become the backbone for combination therapy with check point inhibitors in multiple tumor types. The theory that Abraxane converts M2 macrophages to activated M1 cells has now been confirmed by independent investigators: *"Macropinocytosis of Nab-paclitaxel Drives Macrophage Activation in Pancreatic Cancer."(Cancer Immunology Research, 2017, Pg. OF1-OF9)* In October 2010, Celgene acquired Abraxis BioScience and by 2017 achieved blockbuster status for Abraxane in the treatment of breast, lung, and pancreatic cancer.

To continue the quest of chemotherapy as immune-modulatory agents Dr. Soon-Shiong published and patented the use of Abraxane in a low dose metronomic form in 2010. The efficacy of Abraxane in this low dose metronomic form combined with checkpoint inhibitors was validated in the New England Journal of Medicine publications in 2018 in studies on patients with triple negative breast cancer "*Atezolizumab and Nab-Paclitaxel in Advanced Triple-Negative Breast Cancer."(The New England Journal of Medicine, 2018, Pg. 1-14)* and in patients with lung cancer *"Pembrolizumab plus Chemotherapy for Squamous Non–Small-Cell Lung Cancer."(The New England Journal of Medicine, 2018, Pg. 1-12)*

With the sale of APP and Abraxis in 2011, Dr. Soon-Shiong was free to pursue the concept of a cancer memory vaccine and founded NantWorks to bring this concept to the clinic. He developed the whole genome DNA–RNA next generation sequencing test (GPS Cancer) in order to elucidate the tumor associated antigens and neoepitopes, unique to each individual patient. This test received CLIA/CAP in 2015. Five seminal patents were issued covering the discovery of neoepitopes using the GPS Cancer test (*US 9,646,134; US 9,652,587; US 9,721,062; US 9,824,181; US 9,262,719*). In 2016, NantHealth (Nasdaq: NH) completed its IPO to launch GPS Cancer.

Next was the development of an off-the-shelf Natural Killer cell in order to establish a universal activated and targeted NK cell. With the discovery of a

natural killer cell line (NK92) Dr. Soon-Shiong developed a GMP method to produce a cryopreserved, high affinity CD16 natural killer cell (haNK), forming the bases for the second element of the cancer vaccine and launched NantKwest (Nasdaq:NK).

Finally, to deliver the antigens identified by GPS Cancer at NantHealth and to supplement the off-the-shelf haNK cells at NantKwest with the patient's own CD4, CD8 T cells and NK cells, Dr. Soon-Shiong founded an immunotherapy company beyond checkpoints, NantCell. In 2015, NantCell was launched and developed immunotherapy platforms including the adenovirus virus and yeast delivery systems, cytokine fusion proteins, monoclonal libraries and novel methods to manufacture of primary NK and T cell on a personalized basis for a single patient utilizing an automated "GMP in the box." These technology platforms form the basis of NantCell, the immunotherapy company current enrolling patients in registration trials for 15 indications in cancer.

With the clinical advances across multiple tumor types accomplished at NantCell, the company is now poised to harness the technologies developed at the public entities, NantHealth and NantKwest. The adenovirus and yeast vector delivery systems in NantCell complements the tumor associated antigen and neoepitope discovery engine (GPS Cancer) developed by NantHealth, enabling the subcutaneous delivery of the neoepitopes in the cancer vaccine. The bispecific fusion cytokine proteins of NantCell stimulates the patient's *autologous* NK and T cells, thereby supplementing the *off-the-shelf* cryopreserved haNK cells developed by NantKwest. Collectively the immunotherapy platforms in NantCell, NantHealth and NantKwest serve as a comprehensive path to the development of a cancer vaccine.

About the Evolution and Financial History of NantCell:

In the early 1990s, Dr. Soon-Shiong invented the drug Abraxane, the nation's first human protein (albumin) nanoparticle to activate a specific receptor on the blood vessels supplying the tumor and began the journey of seeking to transform the tumor microenvironment and activating the immune system. Abraxane was approved by the FDA for metastatic breast cancer in 2005, lung cancer in 2012 and pancreatic cancer in 2013. Abraxane is now approved in many countries across the globe with annual sales of approximately $1.0 billion.

From 1997 to 2010, Dr. Soon-Shiong served as founder, Chairman and Chief Executive Officer of two public pharmaceutical companies, American Pharmaceutical Partners, Inc. (NASDAQ: APPX) and Abraxis BioScience, Inc. (NASDAQ: ABII). In June 1998, APPX acquired Fujisawa USA, Inc.'s generic injectable pharmaceutical business to invent manufacturing processes for the first human albumin nanoparticle delivery system. In December 2001, Dr. Soon-Shiong successfully completed an IPO of APPX at a valuation of approximately $769 million. In November 2005, following the approval of Abraxane, APPX announced an approximately $2.4 billion all-stock merger with the privately-held American Bioscience, Inc. to create Abraxis BioScience, combining the strengths of a commercial-stage biotechnology company with a growing injectable pharmaceutical business. In 2007, ABII spun off as a separate entity, with stockholders receiving one share of ABII for every four shares of APPX.

In 2008, Fresenius SE acquired APPX for approximately $5.6 billion inclusive of the full value of a CVR. Each stockholder received $29.00 per share inclusive of the full value of a CVR. In 2010, ABII was acquired by Celgene for approximately $3.6 billion. Each stockholder received, for each share of ABII common stock, a total value of approximately $73.23 per share and one CVR. When the full value of the CVRs are included, the investors in APPX at the time of the Fujisawa acquisition in 1998 would have received a total return of approximately 2,070% and an IRR of approximately 32.4%.

In 2011, Dr. Soon-Shiong founded NantWorks to pursue the concept of a cancer vaccine for all tumor types. He founded **NantHealth** in 2016 to develop the genomic discovery engine for tumor associated antigens and neoepitopes and announced Cancer Breakthrough 2020 vision.

In 2015 Dr. Soon-Shiong launched **NantKwest** to establish the world's first off-the-shelf cryopreserved universal NK cell line.

In May 2015 he founded **NantCell**, with an initial investment from Celgene, whose goal is to employ a broad portfolio of biological molecules that will enable it to develop a cancer vaccine to combat multiple tumor types without the use of chemotherapy. NantCell has one of the most comprehensive late stage clinical pipelines of an integrated platform of technologies addressing both the innate (activated macrophage and natural killer cells) and the adaptive immune system (dendritic, CD4 and CD8 killer T cells). Currently, NantCell is actively enrolling patients for registration trials in 15 indications. In December 2018, Celgene completed a crossover funding round of $30 million at a $4 billion valuation, bringing its overall investment in the company since its inception in 2015 to $105 million and 2.8% ownership in the Company. On January 3, 2019, Celgene announced that it will be acquired by Bristol-Myers Squibb for $74 billion.

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For more information please visit NantCell.com

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Media Contact:

Jen Hodson
NANT
562-397-3639
Jen@nant.com