First targeted nanomedicine to enter human clinical studies

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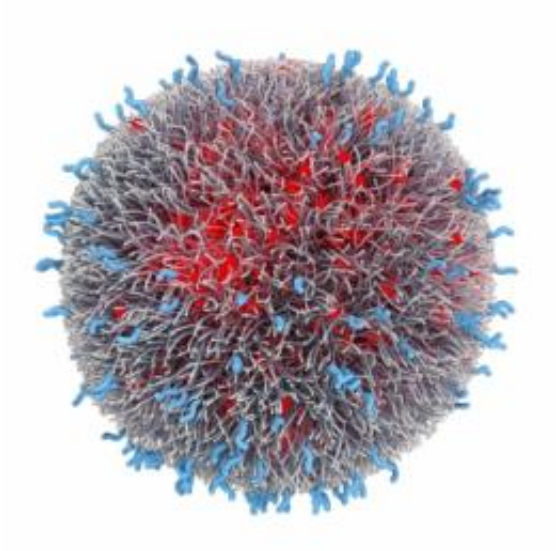

An artist's rendering of BIND-014. Image: Digizyme, Inc.

A team of scientists, engineers and physicians from Brigham and Women's Hospital (BWH), Dana-Farber Cancer Institute (DFCI), Harvard Medical School (HMS), Massachusetts Institute of Technology (MIT), BIND Biosciences, Translational Genomics Research Institute (TGen), Wayne State University Karmanos Cancer Institute, and Weill Cornell Medical College have found promising effects of a first-in-class targeted cancer drug called BIND-014 in treating solid tumors.

BIND-014 is the first targeted and programmed nanomedicine to enter

human clinical studies. The study will be electronically published in *Science Translational Medicine* on April 4, 2012.

In the study, the researchers demonstrate BIND-014's ability to effectively target a receptor expressed in tumors to achieve high tumor drug concentrations, as well as show remarkable efficacy, safety and pharmacological properties compared to the parent chemotherapeutic drug, docetaxel (Taxotere).

"BIND-014 demonstrates for the first time that it is possible to generate medicines with both targeted and programmable properties that can concentrate the therapeutic effect directly at the site of disease, potentially revolutionizing how complex diseases such as cancer are treated," said Omid Farokhzad, MD, a physician-scientist in the BWH Department of Anesthesiology, associate professor at HMS, and study co- senior author.

"Previous attempts to develop targeted nanoparticles have not successfully translated into human clinical studies because of the inherent difficulty of designing and scaling up a particle capable of targeting, long-circulation via immune-response evasion, and controlled drug release," said Robert Langer, ScD, David H. Koch Institute Professor, MIT and study co-senior author.

According to the researchers, the drug is the first of its kind to reach clinical evaluation and demonstrates a differentially high drug concentration in tumors by targeting drug encapsulated nanoparticles directly to the site of tumors. This leads to substantially better efficacy and safety.

In the study, the researchers produced data that include pharmacokinetic characteristics consistent with prolonged circulation and controlled drug release with plasma concentrations remaining up to at least 100-fold

higher than conventional docetaxel for over 24 hours, as well as up to a 10-fold increase in intratumoral drug concentrations with prolonged and enhanced tumor growth suppression in multiple tumor models compared with conventional docetaxel.

Moreover, initial clinical data in a heavily pretreated patient population with 17 patients with advanced or metastatic solid tumor cancers indicated that BIND-014 displays pharmacological characteristics consistent with preclinical findings of differentiated pharmacokinetics and accumulation at tumor sites with clinical effects seen at doses as low as 20 percent of the normally prescribed docetaxel dose and in cancers in which docetaxel has minimal activity (e.g., cervical cancer).

"The development of BIND-014 demonstrates that drug properties such as solubility, metabolism, plasma binding, biodistribution and target tissue accumulation will no longer be constrained to the same extent by the drug chemical composition. It will also become the function of the physicochemical properties of nanoparticles. This will allow for an unprecedented ability to make better medicines for our patients as demonstrated by our emerging clinical data." said Farokhzad.

The researchers note that while the science and technology of BIND-014 builds upon docetaxel's mechanism of action, the emerging evidence is that BIND-014 significantly changes the biological effects of docetaxel by virtue of fundamental changes in pharmacology including major increases in tumor concentration.

To date, the researchers note that BIND-014 has been administered at doses of up to 75 mg/m2 and dose escalation is ongoing. It has been well-tolerated with no new toxicities observed.

"It has been a privilege to be a part of the team that developed this technology at its conception through its clinical translation. The

emerging BIND-014 clinical data showing signals of efficacy even at relatively low doses validates the potential for the revolutionary impact of nanomedicines and is a paradigm shift for the treatment of cancer." said Philip W. Kantoff, MD, Chief Clinical Research Officer at DFCI, Professor of Medicine at Harvard Medical School, and study co-author.

"It is wonderful to witness a world-class team of scientists, engineers, physicians, for-profit and non-project organizations converge to develop this potentially revolutionary technology for treatment of cancers. The effectiveness of this team has been remarkable and serves as model for translational research" said Edward J. Benz, Jr. MD, President of DFCI, Richard and Susan Smith Professor of Medicine at Harvard Medical School.

The research and development of the first targeted programmable nanomedicine to show anti-tumor effects in humans represents the culmination of more than a decade of investigation initially carried out in academic labs at BWH and MIT, and supported by funding from the National Cancer Institute, National Institute of Biomedical Imaging and Bioengineering, The David H. Koch Institute for Integrative Cancer Research at MIT, the Prostate Cancer Foundation, philanthropic gift from David H. Koch, and the Dana-Farber Harvard Cancer Center Prostate Cancer SPORE; and subsequently carried out in the laboratories of BIND Biosciences leading to the development of BIND-014, and supported by funding from the National Cancer Institute, National Institute of Standards and Technology and BIND Biosciences.

BIND Biosciences was launched in 2007 based on technologies that were licensed from BWH and MIT and developed, respectively, in the laboratories of Drs. Omid Farokhzad and Robert Langer, co-founders of BIND Biosciences, the biopharmaceutical company responsible for developing BIND-014.

Provided by Brigham and Women's Hospital