

News

Biothera harnesses innate immune system to fight cancer

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"Imprime PGG®, if properly developed, could be the number one selling anticancer therapeutic of all time," according to Dan Conners, president of Biothera Pharmaceutical Group. His assessment is based on the drug's Phase II results, its novel mechanism of action and its ability to function as a platform therapeutic for a wide range of cancers.



Dan Conners, President, Biothera Pharmaceutical Group

With enrollment underway for Phase III trials, Conners said the technology platform is proven. Biothera already has treated more than 275 patients in studies involving metastatic colorectal cancer, KRAS mutant colorectal cancer, non-small cell lung cancer, and chronic lymphocytic leukemia, with meaningful improvements in all endpoints, "including response rate, progression-free survival and overall survival," he pointed out. Therefore, the major hurdle today isn't technological. The hurdle is to obtain financing to advance the drug through the remaining trials and into commercialization.

The drug

Unlike most other anticancer therapies, Imprime PGG works with the body's innate immune system to enhance its functionality so that it is capable of targeting tumor cells. The historic obstacle to that approach has been that the immune system only attacks pathogens it recognizes as foreign. Tumor cells, because they are formed by the body, aren't foreign and do not trigger an immune response. Imprime PGG resolves that issue. This novel carbohydrate drug harnesses the immune system and redirects its natural killing ability so that it becomes a potent cancer-fighting force.

Imprime is an adjunct to monoclonal antibody (MAB) therapy. As Conners explained, "MABs like Erbitux, Avastin and Rituxan...mimic the action of natural antibodies by binding to the cancer cells. This initiates a natural immune response against the tumor and attracts neutrophils and other immune cell populations to the tumor site." Neutrophils comprise between 50 and 70 percent of the body's white blood cells, making them the largest population of cells within the immune system. On their own, "neutrophils aren't involved in the fight against cancer but, when primed with Imprime PGG, they engage and redirect their natural killing response against these previously intractable targets," Conners emphasized.

When Imprime PGG is injected into the body, it binds to a specific receptor on neutrophils, priming them to engage in antitumor activity against antibody-targeted cancer cells. "Imprime PGG doesn't interfere with the natural immune response. It adds to it," he said. Imprime PGG's selective targeting mechanism does not induce broad-based immune activation, which often is linked to adverse reactions. Therefore, Conners elaborated, "Imprime can mobilize an effective antitumor response without the side effects associated with other therapies."

Trials

Biothera's clinical development strategy has focused upon demonstrating Imprime PGG's effectiveness when used with multiple MABs against many different cancer types. "Imprime is immune cell specific,

not cancer specific. Consequently, we believe it could be used to treat most cancers that can be targeted with an antibody," Connors said.

"Results have been consistently positive throughout multiple trials, showing a marked improvement in efficacy," he added. "For example, when Imprime PGG was administered with cetuximab in late-stage KRAS wild-type metastatic colorectal cancer patients, the response rate was 45%, compared to only 17% with cetuximab alone. Likewise, in KRAS mutant metastatic colorectal cancer patients, overall survival increased 40% and one year survival increased 115% with Imprime," Connors reported.

Enrollment in a Phase III trial for KRAS wild-type metastatic colorectal cancer is underway and is expected to be completed within 18 months. "At the end of Phase II meeting with the FDA, we were granted accelerated approval," Connors said. This Phase III trial is enrolling patients in approximately 50 sites through the US, Germany, France and Canada. The trials are attracting leading oncologists at world class institutions, based upon promising Phase II data and Imprime's novel mechanism of action.

Expertise

This platform technology originated at Massachusetts Institute of Technology, but was advanced by Biothera scientists and by research partners in leading academic institutions. Biothera's scientists comprise a world-class team that includes complex carbohydrate chemists and immunologists with expertise in innate immune system modulation.

By focusing on the innate immune system, Biothera is advancing research and development in an area that is new to most large pharmaceutical companies, Connors observed. "The idea of attacking cancer cells with neutrophils activated by a carbohydrate drug is a very novel approach." That approach is yielding results in a variety of areas. In addition to Biothera's more than 40 US patents and patents pending, it is seeing success in assay development. For example, Connors said, "We have developed an assay for carbohydrate chemistry that the American Chemical Society has adapted as the default assay for the chemical industry." And, he continued, "we have outlined analytical methods in peer-reviewed publications that are becoming industry standards."

In addition to its scientific expertise, Biothera also has assembled an experienced management team that has taken drugs through the clinic and to market. Renowned beta glucan researcher Myra Patchen, PhD, is the CSO for Biothera. She previously was the CEO of Sucampo Pharmaceuticals, where she directed the filing of nine investigational new drug applications and one new drug application. Michele Gargano, VP of clinical development, also joined Biothera from Sucampo, where she was in charge of global product development. William Grossman, MD, PhD, Senior VP of R&D, previously was North American medical director for clinical and medical affairs, biotherapeutics/immunology at Baxter Healthcare Corporation

Board members include Alex Giaquinto, PhD, the former Senior VP in charge of global regulatory affairs at Schering-Plough, who served as Chairman of the Regulatory Affairs Coordinating Committee for the Pharmaceutical Research and Manufacturing Association. Other members of the board include respected entrepreneurs and industry consultants.

The company

"Biothera is privately held, and has raised more than USD 120 million—all from accredited angel investors," Connors emphasized. "We have no venture capitalists and no institutional investors. That makes us unique and increases our flexibility in our approach to partnering." Biothera's investors are committed to the technology at the heart of this company. "Our objectives are different than those of venture-backed companies," he stressed. "We believe our technology platform has the opportunity to change the way the world treats cancer, and we recognize the responsibility that comes with that."

"We want to find a partner who shares our belief in the potential of this drug," Connors continued. The goal is to partner with an organization that has both the financial resources and the expertise to help shepherd Imprime PGG through Phase III trials, culminating in regulatory approval. "We are pioneering a new immunotherapeutic approach to cancer that turns conventional wisdom on its head."