

New Acceleron, Celgene Deal Anything But 'Anemic'

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Celgene Corp. will pay \$25 million up front to Acceleron Pharma Inc. plus up to \$217 million more in potential milestones, under a new collaboration agreement between the two companies for the development of an anemia therapeutic.

Summit, N.J.-based Acceleron will proceed with Phase I and II trials of the drug, and Celgene, of Cambridge, Mass., will take the baton for later Phase II and III trials. The new agreement extends an existing partnership between Celgene and Acceleron dating back to 2008.

The most common treatment for many forms of anemia is erythropoietin (EPO), though it has some significant risks and does not work well for some types of anemia.

ACE-536 is an inhibitor of the TGF beta family of proteins, and it acts on a different population of progenitor blood cells during RBC development than EPO.

"There's the potential that with a different mechanism, there may be a different risk-benefit profile than what's seen with EPO," Steve Ertel, senior vice president of corporate development at Acceleron, told *BioWorld Today*.

"ACE-536 is chemically interesting as members of the TGF-beta superfamily of ligands regulate more than 500 target genes and are involved in many cellular functions, including cell growth, adhesion, migration, differentiation and apoptosis," Celgene told *BioWorld Today*. "Based on data presented so far, we believe that ACE-536 promotes robust development of red blood cells in both normal animals and anemia-based models through an EPO-independent mechanism, thus potentially providing a new option in this area."

EPO's risks include cardiac and thrombolytic events. Additionally, Ertel said, in the case of chemotherapy-induced anemia, there's been concern that EPO may cause progression of the underlying tumor.

Concerns about the safety of EPO has limited its use, particularly in oncology settings. And for some types of anemia, it doesn't work well at all. For example, EPO is prescribed for patients with myelodysplastic syndrome, but responses are typically poor.

In the case of thalassemia, EPO does not work well and

is typically not used. The standard of care for thalassemia is periodic transfusion – a therapy that has its own set of risks and drawbacks, including risk of transmission of bloodborne disease.

Acceleron presented data at the American Society of Hematology meeting in December 2009 showing that ACE-536 promotes formation of red blood cells through inhibition of the TGF-beta superfamily. Administration of the drug produced rapid, dose-dependent increases in hemoglobin, hematocrit and red blood cells in animal models.

Acceleron attributes its ability to broker an early stage deal to its existing relationship with Celgene. The two companies partnered in 2008 to develop another hematology entity, ACE-011 (sotatercept). That unusually large agreement called for \$50 million up front, with development and commercialization milestones up to \$510 million. (See *BioWorld Today*, Feb. 21, 2009.)

At the same time, Celgene locked in rights to three discovery programs in bone loss with \$437 million in potential milestones for each program, bringing the deal total to \$1.8 billion.

ACE-011, a Phase Ib compound at the time, was in development to increase bone mineral density, and had been developed with the support of the Multiple Myeloma Research Foundation.

The development focus for ACE-011 seems to have shifted to other indications, but the collaboration is going strong. Celgene and Acceleron began a Phase II/III trial of ACE-011 for chemotherapy-induced anemia in patients with metastatic non-small-cell lung cancer in June, triggering a \$7 million milestone payment to Acceleron. Acceleron also received a \$5 million milestone payment under that agreement in 2008 when it initiated a Phase II trial in multiple myeloma.

Celgene is without a doubt a power player in the hematology field. Its offerings include successful multiple myeloma therapies Revlimid (lenalidomide) and Thalomid (thalidomide). Its programs dovetail nicely with Acceleron's blood cancer and anemia pipeline.

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In addition to ACE-011 and ACE-536, Acceleron is investigating another compound, ACE-041, for multiple myeloma, as well as solid tumors and age-related macular degeneration.

Outside the hematology umbrella, Acceleron has ACE-031 in Phase II for Duchenne's muscular dystrophy, and preclinical compounds ACE-661 for bone loss and ALKS693 for inflammatory disease.

"We've built upon an existing relationship to form a broad anemia relationship with Celgene," said Ertel.

Terms of the new agreement stipulate that Celgene and Acceleron will work together to develop, manufacture and commercialize ACE-536. Acceleron will carry out Phase I and II trials, and Celgene will take over for Phase II and III trials. Manufacturing for Phase I and II trials will be Acceleron's responsibility. Celgene will manufacture drug supplies for Phase III and beyond.

Acceleron will share development expenses through the end of 2012. Celgene will pay for development after 2012. The companies will co-promote the product in North America, with Acceleron eligible for tiered, double-digit royalties on worldwide sales.

Phase I trials are slated to begin "within the next few months," according to Acceleron.

Acceleron's experience challenges the conventional wisdom that only late-stage compounds can land sweet partnership deals. Celgene, in fact, is very interested in early stage deals.

"We have often looked to bolster our own internal discovery efforts with research collaborations of this type. Recall, our initial collaboration with Acceleron and ACE-011 was only in Phase I at its beginnings," Celgene said. "Additionally, we have intriguing research collaborations with

companies like Agios Pharmaceuticals Inc., GlobelImmune Inc. and Array BioPharma Inc. across a range of indications and mechanisms, all in earlier stages of development. We actively look for unique science when partnering, and our continuing collaboration with Acceleron fits this goal."

Celgene paid \$130 million up front in a preclinical collaboration with Agios, \$40 million up front plus \$500 million in milestones to GlobelImmune for access to its cancer drug programs, and \$40 million up front with a \$1 billion deal total with milestones to Array for four discovery targets in the area of cancer and inflammatory disease. (See *BioWorld Today*, Sept. 25, 2007, May 18, 2009, and April 16, 2010.)

Acceleron's \$25 million compares favorably with many similar, single-compound early stage deals between biotech and pharma that have been made in recent months, though it is not as large as some. The industry is seeing many deals with up-front values between \$20 million and \$40 million for early stage compounds. (See *BioWorld Today*, July 8, 2011.)

The largest year-to-date was closed by Glenmark Pharmaceuticals Ltd. and Sanofi for \$50 million up front and a total potential deal value of \$613 million. (See *BioWorld Today*, May 17, 2011.)

Running a close second is French biotech Innate Pharma A/S which signed for \$35 million up front and a potential \$465 million in milestones with Bristol-Myers Squibb Co. for a Phase I cancer antibody. (See *BioWorld Today*, July 7, 2011.)

At the same time, Acceleron's North American co-promotion rights add significant value to the deal. Co-promotion clauses are one way that a biotech can develop the commercial side of its business while still benefiting from a big pharma partnership. (See *BioWorld Today*, March 18, 2011.) ■