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Celgene Pays Acceleron $25M up front under anaemia drug partnership

Celgene is paying privately held Acceleron Pharma $25 million up front under a deal to jointly develop and commercialise ACE-536, a ligand trap that inhibits members of the transforming growth factor- (TGF) beta "superfamily" involved in the late stages of erythropoiesis – the process of generating red blood cells – as a treatment for anaemia.

Acceleron stands to gain an additional $217 million in milestones under the collaboration, which is the second partnership it has formed with Summit, New Jersey-based Celgene, with the first involving another of the Cambridge, Massachusetts-based biotech's experimental anaemia products, ACE-011 (sotatercept), a soluble receptor fusion protein comprised of extracellular domain of the human activin receptor type IIA fused to human immunoglobulin, which entered Phase II/III testing in June in patients with chemotherapy-induced anaemia with metastatic non-small-cell lung cancer.

The companies, which struck their earlier deal in 2008 to develop ACE-011, in which Celgene paid Acceleron $50 million up front, with the potential for the firm to earn up to $1.82 billion more in milestones, may also pursue development of other potential anaemia treatments under the latest partnership, Steven Ertel, senior vice president of corporate development at Acceleron, told *Scrip*.

"As part of the deal we announced today, we are doing a broad commitment with Celgene to develop products for anaemia, so there may be other uncovered research capabilities that would be part of this broad collaboration," he said.

Acceleron CEO Dr John Knopf said his company has uncovered an "exciting new approach to treating disorders of erythropoiesis," and by combining his firm's strengths with Celgene's, the companies will be able to pursue development of molecules to treat a "broad array of underserved diseases and conditions in which patients suffer from anaemia".

Dr Tom Daniel, president of research at Celgene, who called his firm's partnership with Acceleron "strong," said the work his company plans to embark on with ACE-536 is a "natural extension of our strong presence" in hematology.

Indeed, Mr Ertel noted that one of the major forms of anaemia occurs in cancer patients – chemotherapy-induced anaemia.

"There is a lot of overlap in their areas and expertise and that is one of the reasons we have viewed them as a great partner and collaborator in this area," he said of Celgene.

Mr Ertel emphasized that Acceleron's approach to treating anaemia is very different from those used by companies whose products are based on erythropoietin, such as Amgen's Aranesp (darbepoetin alfa) and Epogen (epoetin alfa) and Janssen Biotech's Procrit (epoetin alfa).

While erythropoietin is a "very well-studied growth factor for red blood cells," it is "not the only factor involved in erythropoiesis," he said, explaining that some members of the TGF-beta protein family also are involved in erythropoiesis.

Both ACE-011 and ACE-536 target members of the TGF-beta superfamily, Mr Ertel noted.

"When you look at the development of red cells, they go through various steps," explained Dr Knopf.

Erythropoietin works on one of the earliest steps in the formation of red blood cells, so in conditions where there is a lack of that hormone, products like Aranesp or Procrit can be used to replace it, he told *Scrip*.

But in some anaemia-related conditions, such as myelodysplastic syndromes (MDS), the defect is not in the production of the early precursors but in the latter differentiation stage, Dr Knopf said.

"This latter differentiation stage is actually where our product works, both ACE-011 and ACE-536," he insisted.

And while erythropoietin is used in MDS patients, its effect is "very limited, with maybe 15% of these patients responding," Knopf noted.

But, he said, "we have demonstrated that our product, ACE-536, was able to correct anaemia in a murine model of myelodysplastic".

Given the potential for 85% of the MDS patient population needing more effective treatments, "we believe we will be able to capture the bulk of that," he maintained.

"What we hope to show clinically is that ACE-011 and ACE-536 through different mechanisms will have a different risk-benefit profile than what has been shown with EPO, and that additionally, through a different mechanism, they can work in anaemia conditions where EPO doesn't work very well," Mr Ertel said.

Dr Knopf noted that even though erythropoietin is largely ineffective in treating anaemia in the MDS population, and the drugs are not approved in the US for that indication, sales in that space have approached nearly $1 billion.

"This is why we and Celgene are very excited about the prospects about this particular indication," he said.

Another potential indication the companies may pursue for ACE-536 and ACE-011 is thalassemia, an inherited blood disorder in which the body makes an abnormal form of hemoglobin, resulting in excessive destruction of red blood cells, which leads to anaemia.

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"We will be able to increase the ability of those red cells to differentiate and be an effective treatment for anaemia associated with thalassemia," Dr Knopf said.

"There's the potential for both compounds to have therapeutic utility in each MDS and thalassemia, and now in the context of this broader collaboration, we will be working with Celgene to determine the optimal fast-forward for each of the molecules among a wider array of diseases," Mr Ertel said, although he emphasized that "We haven't got a definitive plan on which molecules and for which diseases".

"That is something we will be working with Celgene over the coming months on," he said.

Dr Knopf said the companies plan to initiate a Phase I trial of ACE-536 within the next few months – making that compound the fourth investigational drug internally discovered and developed to enter the clinic.

Acceleron will be responsible for conducting the Phase I and initial Phase II studies of ACE-536, while Celgene will conduct the subsequent Phase II and Phase III trials. Acceleron will manufacture ACE-536 for the Phase I and Phase II trials, while Celgene will be responsible for the manufacture of Phase III and commercial supplies.

Acceleron will pay a share of the development expenses through the end of 2012, with Celgene responsible for development costs thereafter.

The companies will co-promote the products in North America. Acceleron will receive tiered double-digit royalties on worldwide net sales.

To date, Acceleron has raised about $100 million in venture capital and has garnered about $200 million from its various partnerships, which also includes a deal with Shire inked last September, in which the Basingstoke, UK-based pharma paid $45 million up front under a collaboration to develop ACE-031, a recombinant fusion protein under investigation as a treatment for Duchenne's muscular dystrophy (DMD), and other molecules targeting the activin receptor type IIB pathway, which plays critical roles in regulating the growth of skeletal muscle, Mr Ertel said.

Under that deal, Acceleron could bank up to $165 million in milestones for ACE-031 in the DMD indication and up to an additional $288 million for other indications and molecules, plus royalties on sales.

Acceleron's pipeline also includes ACE-041, a recombinant receptor fusion protein that inhibits angiogenesis by preventing BMP9 and BMP10, members of the TGF-beta protein superfamily, from interacting with the activin receptor-like kinase 1, a type I receptor that is predominantly expressed on proliferating endothelial cells and is required for the development of mature, functional capillary networks.

"This is a molecule we are really terrifically excited about," Dr Knopf said.

Phase I results of ACE-041 in patients with advanced metastatic cancer demonstrated that two patients with head-and-neck cancer had a greater than 29% decrease in their tumour size, he said.

Dr Knopf noted that the firm plans to initiate an open-label Phase IIa study in head-and-neck cancer this fall, with hopes of reproducing those results.

The compound also is being studied in non-small-cell lung cancer, he said.

Acceleron also is developing ACE-661, a product aimed at stimulating new bone formation.

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