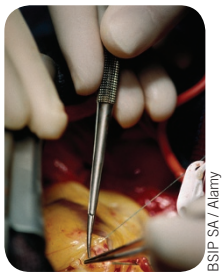
IN brief

Regado's aptamer lines up against anticoagulants



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In September the first reversible antithrombotic drug entered phase 3 clinical trials in patients undergoing percutaneous coronary intervention (PCI). The REG1 anticoagulant system developed by Regado Biosciences, of Basking Ridge, New Jersey, is a two-component therapeutic consisting of a nucleic acid aptamer and its control agent. The combined drugs are pegnivacogin (RB006), a single-stranded 31-nucleotide aptamer that binds and inhibits Factor IXa, and a complementary 15-nucleotide control agent anivamersen (RB007). By adjusting the dose of anivamersen, physicians can release the therapeutic pegnivacogin from Factor IXa allowing coagulation activity to resume. Pegnivacogin is pegylated, with a half-life of more than 24 hours, whereas the control agent anivamersen is metabolized in a few minutes.

Doctors administer strong anticoagulants, most commonly heparin or Angiomax (bivalirudin), during PCI procedures. Because these drugs take several hours to metabolize, the arterial sheath—a plastic tube inserted into an artery to access diseased vessels—remains in place for up to six hours after the procedure to minimize the risk of major bleeding from its removal. With REG1, doctors can dial back pegnivacogin's activity immediately and remove the sheath. "We don't have anything like it in cardiology," says George Dangas, a professor of cardiology at Mt. Sinai Hospital in New York. A reversal agent for heparin exists, but carries significant side effects and no one is eager to use it, Dangas adds. In the phase 2 studies, REG1 was better than heparin at controlling bleeding but there were three severe adverse events in a total of 41 patients treated before the trial was suspended. This turned investors off, says Edward Nash, a biotech analyst at Cowen and Company in New York, although the events were unlikely to be related to the drug. Regado raised only $47 million out of an anticipated $75 million during the company's initial public offering earlier this year. Regado is financing the phase 3 study on its own. The trial will compare REG1 with Angiomax from The Medicines Company, Parsippany, New Jersey, to assess whether the drug is superior in reducing recurrent heart attacks, strokes and the need to revascularize, says David J. Mazzo, CEO. Ritu Baral, a biotech analyst at New York–based Cannacord Genuity rated the company's stock as a 'buy' stating "REG is a highly innovative new anticoagulant that could improve outcomes across a large number of cardiovascular procedures." *Gunjan Sinha*

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Biotech companies are joining the biosimilars game, seeking opportunities beyond Western markets.

pharmaco-kinetic similarity to Enbrel in a confirmatory clinical study in healthy subjects. Coherus aims to meet US, EU and Japanese regulatory requirements, and ultimately to make its products available both in emerging and Western markets, with help from partners along the value chain. In 2012, it signed a deal with Japanese pharmaceutical firm Daiichi Sankyo to develop and commercialize biosimilars of Enbrel and Rituxan (rituximab) in Japan, South Korea and Taiwan. In the Baxter deal, Coherus brought in $30 million upfront, plus up to $216 million in development and regulatory milestones.

Oncobiologics' manufacturing niche is CMC (chemistry, manufacturing and control), where it has assembled a team of experts including founder and CEO Pankaj Mohan. "Biosimilars isn't a viable model for small companies" on their own, notes Mohan, echoing the views of his peers, "so we're focused on CMC and our partners will add the remaining clinical and commercial elements." Armed with biosimilar Humira on the cusp of clinical trials and four other candidates behind (Avastin, Rituxan, Herceptin and Erbitux (cetuximab)), Oncobiologics recently chose to partner with inVentiv Health of Burlington, Massachusetts, for its clinical development and bioanalytical expertise, and for commercial and regulatory support in certain markets. In countries like China and India, a local collaborator is crucial, hence Oncobiologics' agreements with Zhejian Huahei in China, and more recently an Indian firm for the Humira biosimilar in rheumatoid arthritis.

Huahei isn't just licensing Chinese rights, it's also funding Oncobiologics' four biosimilars through the end of phase 1, and taking an equity stake in these assets. Sharing risk (and reward) means Oncobiologics "has enough money to move the company forward" says Mohan.

Because Oncobiologics' CMC packages are designed to meet the European Medicines Agency's and the US Food and Drug Administration's standards, local emerging-market players will be offered high-quality technology and know-how at a relatively low cost, and will thus be in a position to compete aggressively on price. And Oncobiologics may also compete in Western markets such as the UK, where Mohan reckons the company could be among the first wave of entrants with Humira and Avastin (bevacizumab) in 2017 and 2019, respectively.

In markets including the Middle East and North Africa, where EU- and US-standard approval and price matter more than a local partner, Oncobiologics plans to strike supply deals at a later stage. In Southeast Asia, with its growing economies, the company may hold onto rights for itself, especially if it decides to invest in a local manufacturing facility. "That way we'd already be invested and known locally, and be in a position to leverage that," Mohan says.

Despite choosing their target markets and partnership strategies carefully, companies still face significant risk in emerging markets (**Box 1**). Regulations and trade barriers are unpredictable; local bias can be company-specific