or trends to suggest that treatment with FG-4592 is associated with increased risk of cardiovascular events, thrombosis or increases in blood pressure,” said Richard Lafayette, clinical chief of nephrology at Stanford University School of Medicine and chair of the independent Data Safety Monitoring Committee at Stanford, when the phase 2b data on FG-4592 were reported.

Other companies with HIF-PH inhibitors in development are Akebia Therapeutics, and Palkion. On April 5, Akebia announced results from a randomized, double-blinded, placebo-controlled, phase 2, dose-ranging study, reporting that AKB-6548 met the primary endpoint of a dose-responsive increase in hemoglobin from baseline.

Taking a different tack, Acceleron's sotatercept is a soluble fusion protein that binds to activin A, blocking signaling through the activin receptor type 2a. This has the combined effect of boosting red blood cell production and stimulating bone formation (although as yet, the mechanism of action in erythropoiesis is not fully understood). With the backing of its heavyweight part-

ner Summit, New Jersey-based Celgene, Acceleron has advanced sotatercept to phase 2 in treating anemia caused by chronic kidney disease and a phase 2/3 trial in treating chemotherapy-induced anemia in lung cancer.

“That it has taken so long for alternative approaches and targets to reach advanced development highlights the dampening effect Amgen’s control of the market and single-minded defense of its monopoly.”

Another approach to treating anemia is being explored by ProMetic Life Sciences of Laval, Quebec, Canada, with PBI-1402, an orally active, lipidic small-molecule sodium caprate, which acts as an ESA through an undisclosed mechanism. Further back in development, Alnylam is

using short-interfering RNA as the basis of a two-pronged approach, silencing both HIF-PH and hepcidin, a gene that limits iron availability.

That it has taken so long for alternative approaches and targets to reach advanced development highlights the dampening effect Amgen's control of the market and single-minded defense of its monopoly has had on the search for new biology for treating anemia. But even without the emergence of alternative pathways, patent expiries are about to hit home. In the US, Amgen's four key patents on Epogen expire between August 2012 and May 2015.

The arrival of biosimilar EPOs could, of course, affect Affymax's efforts to build a US franchise as much as they cut into Amgen's huge market. Knapp acknowledges this, but says he does not expect any EPO biosimilar to receive approval before 2015.

Meanwhile, Affymax will be prioritizing market share over profit as it moves to carve out a niche and take aim at Amgen's blockbuster franchise.

Nuala Moran London

Texas legitimizes path around FDA oversight

On April 13, the Texas Medical Board by a vote of 10–4 approved guidelines for the use of investigational drugs, including stem cells, in the practice of medicine. The state is positioning itself as “the world’s leader in the research and use of adult stem cells,” wrote Governor Rick Perry to his medical board last July after receiving a stem cell treatment for an ailing back. The letter was part of an effort on the part of the governor and his henchman in the state legislature, Rick Hardcastle, who suffers from multiple sclerosis and wishes to have stem cell treatments himself, to support such treatments by creating an adult autologous stem cell bank in the state. An amendment calling for such a bank and tasking the state’s Health and Human Services Commission with establishing basic rules regarding its work was passed last July as part of an omnibus Medicaid cost-containment bill (Article 14, SB 7 Medicaid Efficiency Bill). Details of such a bank have yet to appear, but the Sugar Land, Texas-based company Celltex, which provided the cells for Perry’s treatment, may be angling for the job. It was reported in *Newsweek* that the governor’s office changed the wording of the bill from the establishment of “banks” to “a bank.” Although it is not the only stem cell bank in the state, it is arguably the best connected, with the CEO David Eller a Perry contributor, and the physician who gave Perry stem cells, Stanley Jones, chief medical officer. Meanwhile, the newly approved regulations appear to break new ground by allowing physicians to use protocols approved by local institutional review boards in lieu of US Food and Drug Administration (FDA) review. Whereas those members of the board who voted for the regulations believe that they provide needed patient protection, others, like Stanford University stem cell researcher Irv Weissman, see them as “a clever way around the FDA’s appropriate role of overseeing clinical trials.” University of Minnesota ethicist Leigh Turner, who testified before the board prior to the final vote, sees many reasons for concern, among them, the loose use of terminology with regard to stem cells (adult stem cells are not mentioned, let alone any discussion of the kinds of preparations that would be allowed), the varied qualifications and quality of work of institutional review boards, particularly for-profit ones, and the lack of clear rules prohibiting payment for experimental treatments. “What you end up with is kind of [a] tearing away of regulatory review and patient–research subject protections,” says Turner. Members of the board who voted for the measure stand by their decision. “We’re trying to be safe. It’s the wild, wild west right now,” Scott Holliday, an anesthesiologist from Arlington, Texas, told the *Washington Post*.

Governor Rick Perry lends a hand to stem cell therapies.

Jeff Malet Photography/Newscom

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