Mackay. In the same vein, a spate of high-profile research articles demonstrating the potential of zinc-finger nucleases to correct genomic defects in monogenic diseases like hemophilia *(Nature* **475**, 217–221, 2011) show considerable promise. But the US Food and Drug Administration's cautious approach to gene therapy trials means that even under ideal circumstances, the company must run a long and expensive gauntlet to get these experimental treatments off the ground.

At an investor teleconference at the end of its third quarter in 2011, Sangamo reported cash reserves of at least $85 million, which they project as being sufficient to capitalize the next few years' R&D efforts. Sangamo also maintains additional revenue streams through commercial partnerships, including a licensing agreement that enables St. Louis–based Sigma-Aldrich to sell ZFP-related research tools and an arrangement with Dow AgroSciences of Indianapolis, which has enabled that company to use Sangamo technology to generate genetically modified (not necessarily transgenic) crops. Royalties and milestone payments from such arrangements have yielded modest but steady revenues—projected at $10–12 million for 2011—and Sangamo intends to further expand on these licensing agreements in the future, although human medicine remains the priority. "Within these walls, Sangamo will stay almost exclusively focused on therapeutic applications," says Lanphier.

As the only company actively developing ZFP therapeutics, Sangamo retains a remarkable head start. "In terms of a commercial presence, they hold a complete patent portfolio and have for many years," says Mackay. Paris-based Cellectis is working with other classes of engineered proteins, such as meganucleases and transcription activator–like effector nucleases (TALENs) (*Nat. Biotechnol.* **29**, 681–684, 2011) for targeted genome editing in cell biology and agriculture applications, but does not appear to be heavily focused on clinical efforts at present. Barbas also points out that TALENs are still relatively new, and questions remain as to whether they can offer the same strong safety profile that has been demonstrated for ZFPs in humans.

In the meantime, the jury remains out as to whether Sangamo can find the right indication, right molecule, right clinical trial design and most compelling data package for regulators that will lead to the registration of a completely new kind of therapeutic modality before their cash reserves run dry. "We're certainly not where we would be if the data had been positive," says Lanphier, "but you go forward with what you have and you do it for the right reasons, and when your expectations aren't fulfilled, you just have to start up the hill again."

Michael Eisenstein, ***Philadelphia, Pennsylvania***

Enbrel patent surfaces

Bloomberg via Getty Images

Extra patent protection for Enbrel could keep cheaper versions off the market until 2029.

Amgen has received another 17 years of patent protection on its blockbuster autoimmune drug Enbrel (etanercept)—which could mean that it will be on the market for 30 years before it faces competition from biosimilars. The patent (US8,063,182) came in November 2011 and was a surprise to many in industry; Merck, of Whitehouse Station, New Jersey, had already announced plans to develop and commercialize a biosimilar version of the drug, plans that are now likely to be shelved.

Enbrel is a recombinant human tumor necrosis factor (TNF)-alpha receptor fused to an IgG fragment that inhibits tumor necrosis factor signaling. Its approval in 1998 for the treatment of rheumatoid arthritis was followed by several other approvals for autoimmune diseases. With global projected sales of $7.8 billion in 2011, the drug is a key product for Amgen of Thousand Oaks, California, and Pfizer of New York, and the world's biggest-selling biologic.

Amgen was granted this unexpected stretch in patent protection because its '182 patent was filed in May 1995 under old rules that applied to patents filed before mid-1995. Those rules, which have now lapsed, awarded patents 17 years from the date of issue. This means the new patent will expire in November 2028. Current standards give patents 20 years from the date of filing.

The 16-year delay between the filing of the '182 patent and its issuance is probably due to a combination of a heavy workload and the backlog at the Alexandria, Virginia–based US Patent and Trademark Office (USPTO). According to Leslie Meyer-Leon, a patent attorney at IP Legal Strategies Group in Boston, who specializes in biotech patents, Amgen itself is unlikely to be culpable for the delay. "I don't think Amgen acted in a way that unfairly manipulated the system; if anyone is at fault in having this patent issued so late, it is the USPTO. Because of inadequate funding, they have a huge backlog of pending applications, especially for those applications whose initial rejection is appealed [which happened with the '182 patent] and so it can take a very long time for a patent to issue." Meyer-Leon notes that the slow pace of patent prosecution can still occur under the current system.

Another change in US patent legislation has played in Amgen's favor. In 2000, the USPTO began to make pending patent applications publically available, and Amgen's filing preceded this. "The issuance of this patent has shock value "because the application was filed at a time when applications were not published and the prosecution records are not available online; thus, there is a surprise factor…." says Meyer-Leon. Some commentators believe it is unlikely there are many patents still pending entitled to a 17-year term from issuance *(Nat. Rev. Drug Disc.* **11**, 9, 2012).

It had been anticipated that Enbrel would be subjected to generic competition soon after another key patent protecting Enbrel (US5,610,279) expired in October of this year. Indeed, in June 2011 Merck struck a deal worth up to $720 million with the Seoul, South Korea, company Hanwha Chemical to develop and commercialize HD203, a biosimilar version of Enbrel, in phase 3 trials that aim to show safety and equivalence in patients with rheumatoid arthritis. Merck has not commented on whether it intends to challenge the new Enbrel patent.

Charlotte Harrison, ***Canterbury, UK***

IN their words

"As a parent, even worse than having no [treatment] prospects was having a prospect that was going nowhere." Tracy Seckler, a former middle-school English teacher whose 11-year-old son, Charley, has Duchenne muscular dystrophy (MD), on why hers and another family with an MD child bought the rights for $500,000 to an experimental drug, halofuginone, dropped by Collgard Biopharmaceuticals of Israel. (*Wall Street Journal*, 27 December 2011)

"At the price of crude oil today, we are able to compete with oil-based paraxylene now." Virent chief executive Lee Edwards, speaking of Coca Cola's recently announced deals with Virent and two other biotechs (Gevo and Avantium) for plant-derived plastic for its nonrecyclable bottles. (*Reuters*, 22 December 2011)