IN brief

Check a patent at WIPO

Finding patents available for licensing internationally became much easier in January as the World Intellectual Property Organization (WIPO) launched a new feature on its PatentScope website. Inventors who apply under the Patent Cooperation Treaty (PCT) may now fill out a "request for indication of availability for licensing purposes" form so that relevant information—such as whether licenses sought are exclusive or nonexclusive and the countries in which the invention is eligible for licensing—can be added to the search criteria within the site. The WIPO program is voluntary for now; however, the US Patent and Trademark Office is currently weighing making licensing availability mandatory for future patent applications. Vedder Price patent attorney Thomas Kowalski notes that not-for-profits and commercial ventures all look to license, partner and monitor, and from this perspective, the WIPO program is an opportunity to disseminate the availability of published patent-pending technology. It could be more useful, he says, if "the information could be published with the PCT publication of an application so the interested public, when viewing a PCT publication, could readily know if the technology is available, rather than need to check a particular website." As of now, the data are accessed through links on the application's "bibliographic data" and "documents" pages. *Michael Francisco*

RNAi patent win

The US Patent and Trademark Office has issued a patent fundamental to RNA silencing to a UK tech transfer firm. The new patent awarded to Plant Bioscience Limited (PBL) of Norwich for discoveries in plants made by David Baulcombe, University of Cambridge, and Andrew Hamilton, University of Glasgow, is likely to affect ongoing industrial research, gene therapeutic products and commercial silencing kits for many organisms including humans. This patent (US 8,097,710) is the third and broadest issued to date based on the initial invention (*Nat. Biotechnol.* **28**, 300, 2010). Jan Chojecki, managing director of the part-publicly funded PBL, says companies have already come forward to purchase a license under the new terms, which covers the use of RNA strands of 20–24 base pairs in length. PBL will grant licenses to US-based industry but has a stated policy not to enforce rights in academia. The terms are flexible, he adds, so the patent should not block innovation. "We are here to see fair recognition of a public-sector innovation, and to ensure that resources come back into UK science," says Chojecki. Scott Lloyd, a patent attorney and analyst at Nerac of Connecticut, points out that the use of 3-prime overhangs on RNA strands, which are already widely used to enable efficient silencing in human cells, is not described in the patent, so companies developing human therapeutics may have a defense against the need to license with PBL. *Jennifer Rohn*

Table 1 Selected cystic fibrosis drugs in late-stage development

Drug	Lead company	Target	Development status
Aeroquin	Aptalis Pharma	Topoisomerase II (DNA gyrase) and IV	Phase 3
Arikace	Insmed	Cell wall synthesis, protein synthesis	Phase 3
Ataluren	PTC Therapeutics	RNA translation	Phase 3
Bronchitol	Pharmaxis	Osmosis	Phase 3
Podhaler	Novartis AG	Protein synthesis	Phase 3

biotech firms to find out if any would take on the project. Only two called him back and one of those, Genzyme, also based in Cambridge, Massachusetts, dropped the project just a few years later.

Vertex acquired Aurora primarily for its chemical screening technology and executives were initially hesitant to pick up an orphan drug project that might distract them from their ongoing efforts with greater market potential, such as hepatitis C. In the end, it was support from the CFF that convinced Vertex to take a chance on the orphan disease by partially shouldering the risk of the project to the tune of $46.9 million. The foundation has funneled about $75 million into the development of Kalydeco and VX-809, and stands to collect royalties from Kalydeco sales.

The once chilly climate towards cystic fibrosis drug development has changed as big pharma embraced the rare disease market in recent years, says Beall (**Table 1**). Kalydeco's success has also helped. "There's a lot more interest now that we've got a proof of concept," he says. CFF has recently signed deals with Paris-based drugmaker Sanofi, and with Pfizer, headquartered in New York.

Vertex's decision to keep the cystic fibrosis program may have proven a wise move. Although the company's hepatitis C treatment Incivek was thought to have blockbuster potential, it is used in combination with interferon alpha, a treatment notorious for its unpleasant side effects. Investors have already moved on, Carr notes, setting their sights on a new generation of hepatitis C drugs—nucleotide inhibitors—that dispense with interferon alpha, and may be available in a few years.

In the meantime, Vertex is looking to the 90% of people with cystic fibrosis who have at least one copy of a deletion mutation called *F508del,* which causes CFTR proteins to misfold and eventually degrade. Those few mutant channels that do make it to the cell's surface fail to open properly, much like G511D mutants.

The company has already tested Kalydeco on *F508del* patients, but these showed little clinical effect. Thus, R&D is focusing on two other drugs: VX-809 and VX-661. These compounds known as CTFR 'correctors' allow *F508del* mutant channels to escape degradation and transit to the cell membrane. VX-809 (lumacaftor) is the farthest along in development and is thought to interact directly with CFTR to guide it to the cell's surface. The drug is being tested in phase 2 studies in combination with Kalydeco, which, it is hoped, will allow the *F508del* mutants to open once they make it to the cell surface.

Early results announced last year showed that the combination of VX-809 and Kalydeco reduced sweat chloride—a marker often used to measure CFTR function—in *F508del* patients. But observers note that the decrease in sweat chloride was not as dramatic as the drop produced by Kalydeco in G551D patients. "It's a much less impressive improvement," says Samuel Moskowitz, a pediatric pulmonologist at Massachusetts General Hospital in Boston. "Dealing with misfolded proteins is likely much more tricky than fixing a gating mutant." Eric Olson, vice president of the cystic fibrosis franchise at Vertex, counters that it is too soon to judge how well the combination therapy works.

Another study, enrolling patients now and expected to report results by the middle of the year, will test a higher dose and longer duration of the drug: 28 days as opposed to only 7. Meanwhile, says Olson, it is not known if sweat chloride scales linearly with clinical benefit. Nevertheless, Vertex is continuing to test its other corrector, VX-661, and many believe that a combination of three or even more drugs may be necessary to overcome the high hurdle set by the *F508del* mutation, says Steven Rowe, a pediatric pulmonologist at the University of Alabama at Birmingham.

Financial analysts will be watching the performance of Vertex's correctors closely. They expect the newly approved Kalydeco to bring in less than $1 billion a year even if the label is expanded to cover younger patients and other gating mutations. "It's important to see where the growth is beyond that," says Carr. "We're interested to see whether or not they expand into that *F508del* population."

Heidi Ledford, *Cambridge, Massachusetts*