

PHILANTHROPY

Charities seek cut of drug royalties

Non-profits that support medical research are angling for a share of the proceeds and intellectual-property rights.

BY HEIDI LEDFORD

“The Plant Pest Act was completely inappropriate for regulating biotech crops, but the USDA jury-rigged it,” says Bill Freese, science-policy analyst at the Center for Food Safety in Washington DC. “Now we can foresee this loophole getting wider and wider as companies turn more to plants and away from bacteria and other plant-pest organisms.” The USDA has not made public any plans to close the loophole and has also indicated that it will not broaden its definition of noxious weeds, a class of plants that falls under its regulatory purview, to facilitate the regulation of GM crops.

Nevertheless, *Agrobacterium* is still industry’s tool of choice for shuttling in foreign genes, says Johan Botterman, head of product research at Bayer BioScience in Ghent, Belgium. The technique is well established for many crops, and particle bombardment is less predictable, often yielding multiple, fragmented insertions of the new gene.

But *Agrobacterium* isn’t suitable for some new techniques. Many companies are developing ‘mini-chromosomes’ that can function in a plant cell without needing to be integrated into the plant’s genome. Last summer, agribusiness giant Syngenta, based in Basel, Switzerland, conducted the first field trials of maize (corn) containing engineered mini-chromosomes, and showed that the mini-chromosomes, which carried multiple genes for insect and herbicide resistance, were stable in the field. “I would expect that by the end of the decade, this technology will be well used by many as a way to deliver large stacks of genes to plants,” says Roger Kemble, head of technology scouting for Syngenta.

Other techniques under development insert foreign genes into designated sites in the genome, unlike the near-random scattering generated by *Agrobacterium*. In 2009, researchers at Dow AgroSciences in Indianapolis, Indiana, and Sangamo BioSciences in Richmond, California, announced that they had used enzymes called zinc-finger nucleases to insert a gene for herbicide resistance at a specific site in the maize genome (V. K. Shukla *et al.* *Nature* 459, 437–441; 2009). Bayer is interested in harnessing other enzymes called ‘meganucleases’ to do the same type of targeted engineering, a strategy that Botterman says may make it possible to introduce multiple new traits into existing GM crops.

Regulators need to adapt to these new techniques, or run the risk of over- or under-regulating GM plants, says Roger Beachy, a plant biologist at Washington University in St Louis, Missouri, and former head of the USDA’s National Institute for Food and Agriculture. The Kentucky bluegrass decision drives this point home, he says: “It really speaks to the importance of reviewing the regulatory process periodically to ensure that it is keeping up with the advances in technology.” ■ **SEE EDITORIAL**

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Early next year, a drug for cystic fibrosis is expected to come before the US Food and Drug Administration for approval. It is a moment that the Cystic Fibrosis Foundation (CFF) will have waited 12 years and invested US\$75 million to witness. Approval of the drug, VX-770 — developed by Vertex Pharmaceuticals of Cambridge, Massachusetts, with support from the foundation — would provide a new treatment for patients, and a revenue stream for the charity.

The CFF, based in Bethesda, Maryland, has a stake in the intellectual property underlying VX-770, and is entitled to royalties from sales of the drug. Such ‘venture philanthropy’ is increasing among charities. Like venture capitalists, non-profit groups are managing research projects, making funding dependent on the projects reaching predetermined milestones and potentially reaping a financial return. They are also keeping control over the fruits of their investment in case the journey from lab to treatment encounters obstacles.

“Philanthropies are looking to have more of a hand in managing intellectual property,” says Timothy Coetzee, chief research officer of the National Multiple Sclerosis Society in New York, and former president of Fast Forward, the society’s venture-philanthropy arm. Philanthropic donations for medical research are increasing (see ‘Growing influence’), even as government granting agencies tighten their purse strings and venture capitalists cut back on biotechnology investments. As a result, non-profits have more bargaining power than ever before — especially for early-stage, high-risk projects that tend to be unattractive to private and federal investors.

“The charities are providing funds at the time when the risk is the very highest,” says Ken Schaner, an attorney at Schaner & Lubitz — a law firm in Bethesda, Maryland, that specializes in working with non-profit

organizations. “But yes, they expect a return.” The CFF is not alone: charities including the ALS Association in Washington DC, the Muscular Dystrophy Association in Tucson, Arizona, and the Wellcome Trust in London have also demanded royalties from some projects. Schaner says that the value of the return often depends on the size of the investment — for example, a foundation might be entitled to six times its input. In some cases, Schaner estimates that the payout could be as much as \$1 billion.

But organizations aren’t interested only in generating revenue for their charitable work. Their involvement also helps to ensure that therapies reach the people who need them, in case anything happens to the drug companies with which they are collaborating.

In 2000, Schaner worked with the CFF to carve out a deal with Aurora Biosciences in San Diego, California — a pharmaceutical company that was later sold to Vertex — to develop the drug that was to become VX-770. The deal was one of the first examples of venture philanthropy.

But Schaner says that he couldn’t sleep the night after the deal was signed. “I started thinking about what would happen if Aurora lost interest in the project. It could just sit there on the shelf untouched,” he says. So he created an ‘interruption licence’ that is now used widely to give charities the intellectual-property rights behind a project if a company abandons it. ▶

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GROWING INFLUENCE

Donations from charities to US biomedical research have tripled in the past decade.



SOURCE: FOUNDATION CENTER

▶ Those rights came in handy in another deal. The CFF had invested about \$25 million in a recombinant enzyme that could treat pancreatic deficiencies in people with cystic fibrosis. When the developer, Altus Pharmaceuticals in Waltham, Massachusetts, confessed that it could not afford a phase III clinical trial, the foundation snatched up the licence to the patent and shopped around for a new taker.

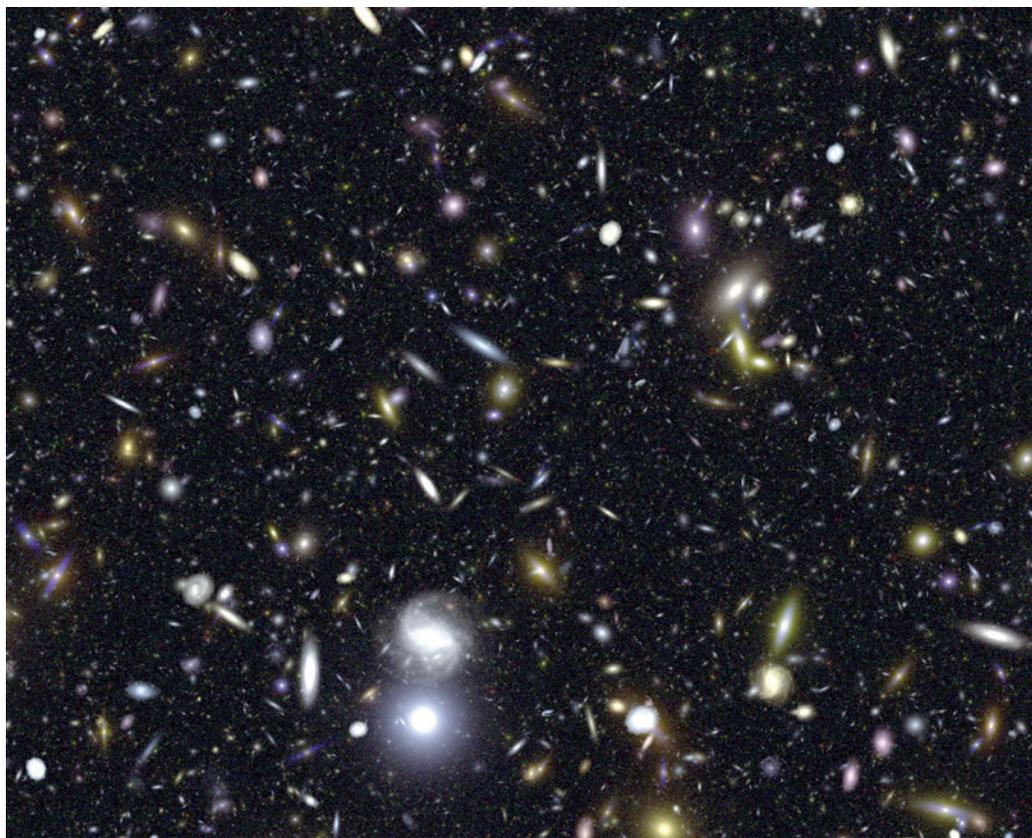
The technology ended up with Eli Lilly, a drug firm based in Indianapolis, Indiana. The foundation then sold off its royalty rights, funnelling the money into another programme. The recombinant enzyme came up for approval this year, but the Food and Drug Administration has requested further clinical trials.

Philanthropic organizations don't always go unchallenged: universities and companies can chafe at handing over intellectual-property rights. "Some philanthropies are getting more aggressive and greedy," says Jeffrey Quillen, a lawyer at the law firm Foley & Hoag in Boston, Massachusetts, who represents start-up companies and university spin-outs. "They see what big pharma gets from these deals and they decide they want stock or co-ownership of intellectual property, too." Some non-profits reduce their intellectual-property demands to ensure that the project doesn't stall because of disputes.

There is also strife when it comes to sharing royalties. "It's tough, but we'll do it sometimes," says Lita Nelsen, director of technology licensing at Massachusetts Institute of Technology in Cambridge. For example, the university might agree "if the foundation shares in the patent costs". Charities, for their part, tend to resist compensating universities for the 'indirect costs' that might result from a grant — which range from utilities to administrative support. That, notes Nelsen, adds to frustration in negotiations. "They think they're giving us money, but they're costing us," she says.

For the charities, royalties can help to fill the void left by the economic crisis. "Traditional fund-raising is still down for us," says Robert Beall, president of the CFF. "We took the Lilly royalties and put them right back into research — that's what we intend to do to make up for the deficit." The foundation reported more than \$53 million in royalty revenues last year.

But despite growing awareness of the importance of royalties and intellectual property, Schaner says that some non-profit organizations still give the issue short shrift. "Often, charities don't think past the first year or two when the grant is being made," he says. "They're so accustomed to clinical failures that they don't put enough emphasis on, 'We might have a success, and what happens then?'" ■ [SEE EDITORIAL P.266](#)



A simulated deep-field image of galaxies like those the James Webb Space Telescope might observe.

SPACE SCIENCE

NASA telescopes face budget abyss

Flagship missions at risk as astrophysics funding shrinks.

BY ERIC HAND

As the space shuttle glides through its final week, another arm of the US space programme faces a bleak future. Astrophysics was once NASA's highest-funded science division and, with the Hubble Space Telescope, a long-time public-relations winner. But its two flagship telescope missions, ranked as the highest priorities for US astronomy, are now under threat as budget constraints start to bite.

Stung by spiralling costs and charges of mismanagement, the James Webb Space Telescope (JWST) — Hubble's long-awaited successor — is now seen by some critics as too expensive to fly. And the Wide-Field Infrared Survey Telescope (WFIRST), which would hunt for exoplanets and probe the poorly understood phenomenon known as dark energy, may take too long to develop to be

worthwhile. Added to that, the astrophysics division is facing a budget crunch while other science divisions within the agency weather the fiscal storm and even come out ahead.

"Clearly there's strong support for science," astrophysics director Jon Morse said at an advisory panel meeting on 13 July as he reviewed his division's place in the scientific pecking order at NASA. "The change here is about priorities."

With support from President Barack Obama, the agency's Earth science budget is at an all-time high. Over the next four months, the planetary science division is due to launch three major missions: to the Moon, to Mars and to Jupiter. And the heliophysics division plans to send a probe plunging into the blistering atmosphere of the Sun, closer than ever before. But because the overall NASA science budget is relatively flat, something had to give. Since 2008, astrophysics funding has plunged