IN brief

AAV gene therapy continues to woo investors

Syncona, the venture arm of London-based charity Wellcome Trust, in January invested £12 ($20) million in an Oxford startup, the first program of which is a gene therapy for inherited blindness. NightstaRx—pronounced 'Nightstar'—is a spin-out from the University of Oxford and its research commercialization unit Isis Innovation. The company is pursuing a therapy for choroideremia (CHM), an inherited X-linked form of progressive blindness, caused by mutations to the gene encoding Rab-escort protein 1 (REP1). The first symptoms occur in childhood with reduced night vision as the retina degenerates. The gene therapy—an adeno-associated viral (AAV) vector encoding REP1 designed to deliver the correct version to the cells in the retina—was developed by Robert MacLaren at Oxford's Nuffield Laboratory of Ophthalmology. Vision improvements achieved by six patients were published in the *Lancet* (doi:10.1016/S0140-6736(13)62117-0; 16 January 2014), and a 12-patient phase 1 trial is underway. If approved, the price for this one-time treatment could fall between $83,000 and $110,000 per quality-adjusted life year, says Sander van Deventer, managing partner for Naarden, The Netherlands–based Forbion Capital Partners, the investors who backed the first FDA-approved gene therapy UniQure. The figures paid out for gene therapies are likely to match those for severe, untreated, Crohn's disease or rheumatoid arthritis, which are on a par with blindness for reduced quality of life, he says. Final payout will depend largely on whether the therapy brings full sight recovery or just restores light perception—and how long it lasts. Another gene therapy company Voyager Therapeutics of Cambridge, Massachusetts, raised $45 million in a series A round from investors Third Rock Ventures in February. Voyager's lead gene therapy program, an AAV serotype 2 vector encoding the dopa decarboxylase gene, is currently in phase 1 trials for Parkinson's disease. *Barbara Cassasus*

IN their words

"I remember when they said, 'By 2014, we'll have the whole human genome in 15 minutes'. At the time, you had to say, 'No, you're not, of course you're not.' They lost their way." Tim Hunkapiller, genomics consultant and brother of Tom Hunkapiller, CEO of PacBIO, commenting on overpromising in PacBio's early days. (*Xconomy,* 3 March 2014)

keep calling," she says. Finally DePaoli, who at the time was global team leader for Amgen's leptin research, convinced higher-ups to supply the drug for trials in patients with lipodystrophy. NIH and UT Southwestern agreed to conduct a two-center study and collaborated with Amgen in writing the trial protocol, which resulted in a 2002 paper on nine patients who improved dramatically (*N. Engl. J. Med.* **346**, 570–578, 2002).

Since then, the drug has changed hands several times. In 2006, Myalept was out-licensed by Amgen to Amylin Pharmaceuticals. Then it became part of the BMS portfolio when BMS acquired the biotech in 2012. Then in February this year, Myalept came under London-based AstraZeneca's control, through a deal transferring BMS's diabetes portfolio to the big pharma.

Myalept works just like its natural counterpart leptin, which acts on hunger centers in the hypothalamus to regulate body weight within a defined range; when leptin is low, appetite increases and vice versa. Over the years leptin has emerged as the most important hormone regulating appetite. "The only hormone that you can obliterate and then you suddenly become an eating machine is leptin," says O'Rahilly.

AstraZeneca plans to pursue drug approval in partial lipodystrophy. One primary limitation of studies to date is a lack of long-term data. "Nobody imagined this would go on for over a decade," says Oral. Moreover, because a pharmaceutical company was not in charge from the beginning, data from the investigator-initiated studies weren't necessarily collected for the purpose of drug approval, she says. Indeed, money spent by companies to develop Myalept for lipodystrophy came largely at the end, she says. With the drug far from a blockbuster, industry's lethargic approach to developing it is partly understandable.

In the future, there may be other conditions that could benefit from leptin therapy. Oral plans to study Myalept in nonalcoholic steatohepatitis, an aggressive form of non-alcoholic fatty liver disease. Based on the drug's mechanism of action, it may also play a role in treating amenorrhea induced by stress or exercise and subtypes of obesity characterized by low leptin. As data builds up, "leptin may gradually realize a broader role in therapeutics," says O'Rahilly. "The history of endocrinology has often been so."

Gunjan Sinha *Berlin*

Cheerios alert

Original Cheerios will no longer contain any genetically modified organisms (GMOs) and will be clearly labeled as such, General Mills announced in January, while still claiming on their website that they support GMO ingredients as safe. Critics say that they bowed to pressure from anti-biotech group GMO Inside, which is now expanding their lobbying to include Honey Nut Cheerios. It remains to be seen whether consumers will pay for the nonmodified cereal if it comes with a heftier price tag in 2014. General Mills has not altered the formulations of any of its other best-selling cereals.

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