# IN brief

## Mitochondrial medicine

Specialty firm Edison Pharmaceuticals of Mountain View, California, has entered a strategic alliance worth up to $4.3 billon with Dainippon Sumitomo Pharma (DSP) of Osaka, Japan, to develop drugs for inherited respiratory chain diseases of the mitochondria. Under terms of the deal, the companies will jointly expand Edison's pipeline, bringing ten new compounds targeting redox pathways into clinical development over the next five years. Also in pursuit of mitochondria-related diseases is biotech firm Mitokyne of Boston, which in October 2013 struck a five-year agreement with Astellas Pharma of Tokyo, potentially worth $730 million, to discover and develop drugs that modulate mitochondrial function. After decades of disinterest from investors, the deals confirm that mitochondrial research is gaining more traction. Douglas Wallace, director of the Center for Mitochondrial and Epigenomic Medicine in Philadelphia, points to a wider acceptance that systemic, cellular-energy metabolism defects caused by mitochondrial mutations can result in organ-specific symptoms and multisystem disorders, such as diabetes and Alzheimer's disease. Wallace, who showed that mitochondrial DNA is inherited exclusively from the mother, says: "I'm hoping we can [persuade other pharmaceutical companies] that mitochondrial bioenergetics is a good target." Hopes of tackling mitochondrial disease were raised on both sides of the Atlantic in February, when the US Food and Drug Administration and the UK government discussed mitochondrial replacement. This *in vitro* fertilization technique involves placing nuclear DNA from a woman with defective mitochondria into a donated egg that has had its nuclear DNA removed and contains healthy mitochondria. In the UK, where there is broad support for such a therapy, the government's Department of Health announced on February 27 that it was opening a three-month public comment period on draft legislation on the technique. At the US Food and Drug Administration, advisory panels discussed what controls might be used in clinical trials, but no decisions were made. *Emma Dorey*

# IN their words

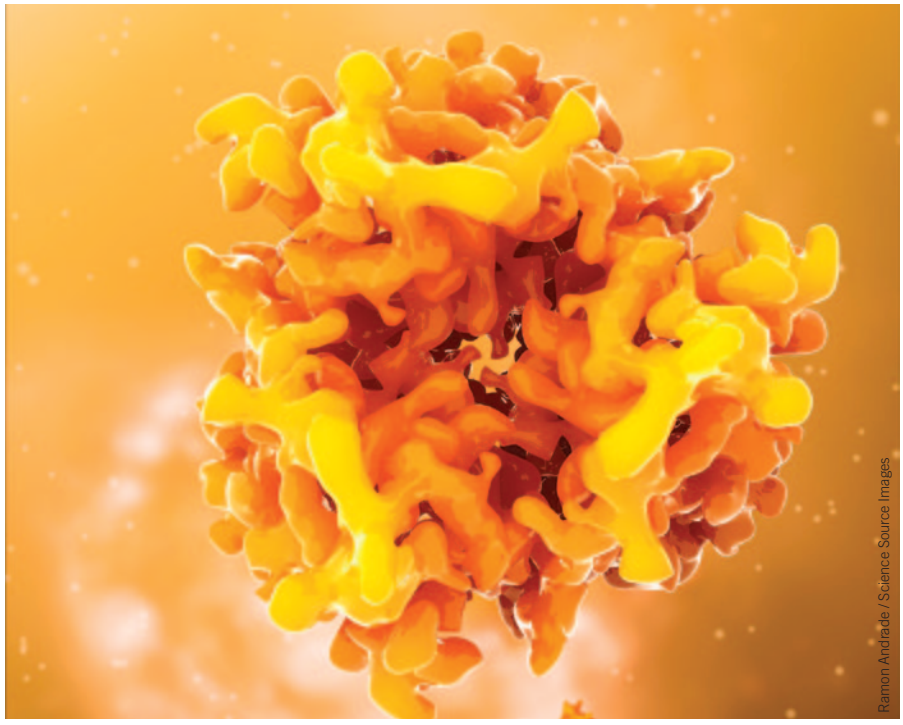
**"Now, people treat us like we're an overnight success. Twenty-five years of overnights is not quite an overnight success."** CEO and founder of Regeneron, Leonard Schleifer, explains how his company came to make him a billionaire. (*Forbes*, 25 February 2014)

# Leptin therapy gains FDA approval

In February, the US Food and Drug Administration (FDA) approved AstraZeneca's Myalept (metreleptin) to treat generalized lipodystrophy—a disorder that affects under 200 people in the US. The approval marks a major milestone in a 20-year odyssey of a drug that almost never was. Myalept is a recombinant form of human leptin, a naturally occurring protein hormone secreted by fat cells. Leptin and its role in controlling satiety, first described in 1994 (*Nature*, **372** 425–432, 1994), ignited a frenzied excitement over the prospect of using leptin replacement therapy to treat obesity. But attempts were abandoned in the late 1990s after studies with obese people failed to show any benefit. It is only thanks to investigator-funded clinical trials and a final push by current sponsor Bristol-Myers Squibb (BMS) of New York that recombinant leptin has wound its way through the FDA to become a lifesaving treatment for a largely neglected indication. "It has been a long and challenging path for metreleptin," says Alex DePaoli, vice president of clinical research at NGM Biopharmaceuticals in San Francisco.

For all the promise once heaped on this hormone, the approval is for a dramatically circumscribed population. Generalized lipodystrophy is a rare disorder characterized by absence of adipose tissue. With no adipose tissue to secrete the appetite-suppressant leptin, individuals with lipodystrophy eat voraciously. The consequences are catastrophic, says Stephen O'Rahilly, director of the University of Cambridge Metabolic Research Laboratories. Excess calories get stored as fat in liver and muscle cells leading to diabetes, high blood lipid levels and pancreatitis. "It's a totally appalling double whammy of being constantly hungry but of food being your greatest enemy," says O'Rahilly. The disease manifests either as generalized or partial lipodystrophy. Both forms can be inherited or induced by medications or result from autoimmune disease or unknown causes.

The generalized form of lipodystrophy is extremely rare. There are fewer than 200 people in the US and 1,000 at most with partial lipodystrophy of varying severity, says Abhimanyu Garg, chief of the division of nutrition and metabolic diseases at the University of Texas (UT), Southwestern Medical Center. Currently there is no treatment other than managing complications. Myalept treatment yields striking results in people with generalized lipodystrophy. It markedly reduces food intake, improves blood glucose and triglyceride levels, in some cases normalizing levels of both.




Leptin, a hormone secreted by fat cells, is now in the clinic, but only a few will benefit from it.