Combined insulin/GLP-1 pens near market

The US Food and Drug Administration's (FDA) advisory committees recommended the approval of two drug combinations of basal insulin with a glucagon-like peptide-1 (GLP-1) receptor agonist for treating adults with type 2 diabetes: one from Bagsvaerd, Denmark–based Novo Nordisk and another from Paris-based Sanofi. The French pharma expected a decision in August for iGlarLixi (insulin glargine/lixisenatide), but the agency pushed the PDUFA date to November, leaving Novo's rival combination iDegLira (insulin degludec/liraglutide) first in line for approval. Trial results show both fixed-dose combinations are more potent than either of their components. But it is unclear whether these therapies containing two agents with complementary modes of action will establish a new paradigm for treating type 2 diabetes. Doctors, patients and regulators now must weigh the potential advantages in patient compliance and fewer injections of these new combined drugs, against pricing, a potential for medication errors and a loss of dosing flexibility.

Novo Nordisk's IDegLira—already approved in Europe under the name Xultophy—combines the company's long-acting insulin Tresiba (insulin degludec) and the GLP-1 agonist Victoza (liraglutide). Similarly, Sanofi's iGlarLixi marries its long-acting insulin Lantus (insulin glargine) with the GLP-1 agonist Lyxumia (lixisenatide). Both could help patients who are unable to achieve glycemic control with current treatments. "Only about 50% of patients can achieve their blood sugar targets in the real world," according to Alan Moses, Novo Nordisk's chief medical officer.

The combination injections were more effective at controlling blood glucose than either drug used alone. In Novo Nordisk's phase 3 DUAL series of trials, IDegLira used for 26 weeks pushed down hemoglobin A1c levels (a marker of glucose control) by 1.9% from baseline compared with 1.4% reduction with long-acting Tresiba and 1.3% drop with the GLP-1 agonist. Sanofi investigated its combination in the LixiLan-L and LixiLan-O trials. In the latter, after 30 weeks, the fixed-dose combination pushed HbA1c down from baseline 1.6% compared with 1.3% with long-acting insulin and 0.9% with the GLP-1 agent alone, respectively. "These drugs are very potent combinations of two very effective drugs," says Michael Nauck, head of clinical diabetes research of Ruhr University in Bochum, Germany.

Combining two or more drugs is not a new idea; the benefits of combination therapy were originally described more than a century ago to treat trypanosomiases (*C. R. Séances Acad. Sci.* **139**, 19–22, 1904). Currently, patients take combination therapies for HIV-1 infections, where poly-pills offer simplicity in the face of complex antiretroviral regimens, such as Brentford, UK–based ViiV Healthcare's Triumeq (abacavir/dolutegravir/lamivu-

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Lars Sorensen, CEO of Novo Nordisk, knows the market for his company's diabetes products will keep growing as a global obesity epidemic tips more people into type 2 diabetes.

Human–animal hybrid ban may end soon

The US National Institutes of Health (NIH) is seeking public comment on proposed changes to the way it funds research into animal embryos containing human cells. The proposal, announced on August 4, would lift a funding moratorium issued by the agency last October on research involving certain types of human–animal chimeras (*Nat. Biotechnol.* **34**, 124–125, 2015). The policy changes are aimed at updating guidelines for funding chimeric animal model research in view of the advances made in stem cell biology. The agency is proposing to set up an in internal steering committee, independent of the peer review process, to monitor new developments in this field and give 'programmatic input' into funding decisions. The committee will advise on two areas: research using human pluripotent cells introduced into nonhuman vertebrate embryos, up through the end of gastrulation (with the exception of nonhuman primates), and research in which human cells are introduced into post-gastrulation nonhuman mammals (excluding rodents) where the animal's brain function might be altered by the human cells. Chimeric organisms comprise admixtures of genetically distinct cells. Early-stage embryo chimeras are deemed to be of more concern that chimeras created using differentiated cells; and chimeras made with tissues from nonhuman primates raise more ethical issues than those based on species more distantly related to humans. The NIH is also proposing to modify current guidelines (set out in 2005 and amended in 2009) to expand a prohibition on the introduction of human pluripotent stem cells into blastocyst-stage nonhuman primate embryos, to include the pre-blastocyst stage. Public comments were due before September 4. In the interim, the blog post from the NIH's associate director for science policy Carrie Wolinetz in which the proposals were described received overwhelmingly negative comments from mostly (what appear to be) nonscientists.

> **"No no no no no no no no. No evidence that the perturbations in the gut microbes are directly influencing anything in the brain. It is a good model. But they need to be more careful with their wording,"** Jonathan Eisen alludes to a study (*Sci. Rep.* **6**, 30028 (2016) doi:10.1038/srep30028) purporting to show that changes in the gut microbiome alter brain chemistry, which was reported by some in the press as curing Alzheimer's disease. (*@phylogenomics*, 22 July 2016)