NEWS IN BRIEF

Merck & Co. drops osteoporosis drug odanacatib

Merck & Co. has discontinued development of its cathepsin K inhibitor odanacatib, citing an increased risk of cardiovascular events for the osteoporosis drug. The decision was an expensive setback for the company: the drug spent 12 years in clinical development and its pivotal trial enrolled more than 16,000 patients.

Researchers first started working on cathepsin K inhibitors in 1995, after discovering that osteoclasts — which resorb bone tissue as part of the continual bone-remodelling process — secrete cathepsin K protease to degrade the bone protein matrix. Currently approved bone strengthening 'anti-resorptive' drugs slow down osteoclast activity through a variety of mechanisms, but in so doing they also lower the activity of bone-building osteoblast cells. By blocking secreted cathepsin K, drug developers hoped they could prevent bone resorption without affecting the ability of osteoblasts to build bone.

Merck's phase III data suggest that odanacatib did indeed have efficacy, increasing bone mineral density and reducing the risk of fractures (*Ther. Adv. Musculoskelet. Dis.* **7**, 103–109; 2015). But it also increased the risk of stroke, the company reported in September at the annual meeting of the American Society for Bone Mineral Research (ASBMR). The mechanistic underpinnings of this risk remain unknown, the company said. There is currently only one other cathepsin K inhibitor in clinical trials: Medivir advanced its MIV-711 into phase II trials for osteoarthritis in January 2016.

Several other cathepsin inhibitors have previously fallen by the wayside. Novartis dropped its balicatib in 2006 because of dermatological adverse events, and GlaxoSmithKline dropped its relacatib in 2007, possibly because of off-target toxicity. Sanofi dropped its dual cathepsin S/K inhibitor SAR114137 in 2012 for undisclosed reasons, but researchers are now studying the drug as a repurposing candidate for Chagas disease under the NIH's New Therapeutic Uses programme.

The osteoporosis community is still excited, however, over the prospects of Amgen and UCB's first-in-class sclerostin-targeting romosozumab, which is currently under review for approval (*Nat. Rev. Drug Discov.* **15**, 445–446; 2016).

Asher Mullard

Cardiovascular pipeline decline quantified

Between 1990 and 2012, the proportion of new cardiovascular drugs entering into clinical trials declined across all stages of clinical drug development, shows a recent pipeline analysis (*JACC Basic Transl Sci.* **1**, 301–308; 2016).

The analysis, by academic researchers from Harvard University, looked at the size of the cardiovascular pipeline compared with the overall pipeline. In the early 1990s, cardiovascular drugs accounted for 16% of phase I candidates and 21% of phase III candidates. In the years running up to 2012, they accounted for 5% of phase I candidates and 7% of phase III candidates.

When the authors drilled down into the novelty of the pipeline, they found a rise in the proportion of phase III cardiovascular drugs with new mechanisms of action. Novel drugs accounted for 27% of the phase III cardiovascular candidates in 1990, and 57% of the candidates in 2012. "The observed contraction in cardiovascular research output may be driven by fewer follow-on drugs," the authors note.

An analysis of progression rates showed that cardiovascular drugs are just as likely to successfully complete clinical trials as other drugs, even in phase III.

"Given the increasing burden of cardiovascular disease globally, the declining pipeline of new therapies is concerning. Policymakers should focus their efforts on supporting research aimed at improving gaps in the understanding of the pathophysiological bases for cardiovascular disorders, as well as facilitating translational efforts to develop new cardiovascular therapeutics," the authors conclude.

The decline in cardiovascular drug development over the past two decades mirrors the decline in central nervous system drug development (*Nat. Rev. Drug Discov.* **14**, 815–816; 2015).

Asher Mullard

New vaccine coalition targets epidemics

A new global vaccine development fund called the Coalition for Epidemic Preparedness Innovations (CEPI) aims to stimulate, facilitate and finance the development of vaccines against infectious disease epidemics.

The CEPI public–private partnership is currently backed by the Bill & Melinda Gates Foundation, the Wellcome Trust, the World Economic Forum, the government of India and the Norwegian government.

The fund was proposed in 2015, in an article co-authored by Wellcome Trust Director Jeremy Farrar calling for a US$2 billion collaboration to foster vaccine development (*N. Engl. J. Med.* **373**, 297–300; 2015). John-Arne Røttingen, interim CEO of the CEPI, told *Science* that the public–private partnership hopes to raise enough money to spend "a couple of hundred million dollars" annually in its early years.

It will initially focus on encouraging the development of two or three as yet unidentified vaccines. Initial priorities could include chikungunya, coronaviruses, filoviruses, Rift Valley fever, West Nile fever, Crimean–Congo haemorrhagic fever and Nipah virus.

The CEPI points out that the most recent outbreak of Ebola killed more than 11,000 people and caused an estimated economic loss of more than US$2 billion. Because epidemics disproportionately affect low-income countries, the CEPI will ensure that any vaccines it helps to develop will be affordable.

GlaxoSmithKline (GSK) has meanwhile proposed launching a 'biopreparedness unit' that would be dedicated to the development of critical but commercially unattractive vaccines. The company has said it is ready to provide a facility, staff and technology, and is looking for funding from public or private entities such as the CEPI. GSK's chairman of vaccines Moncef Slaoui, who is on the CEPI's interim board of directors, has been advocating for a more concerted effort to control potentially epidemic pathogens (*Nat. Rev. Drug Discov.* **14**, 452–453; 2015).

Asher Mullard