NEWS IN BRIEF

R&D spending on the rise

Biotech and pharmaceutical companies boosted their research and development (R&D) spending in 2013.

The lowdown: Ernst & Young reported that biotech spending hit US$29.1 billion in 2013, up 14% from $25.4 billion in 2012 (FIG. 1). "R&D spending rebounded forcefully to return to historic levels for the first time since the start of the global financial crisis," the analysts wrote in their annual report, which looked at 616 biotech companies. A 20% increase in R&D spending in the United States drove the spike. In Europe, biotech spending fell by 4%.

"The amount of capital made available by investors, particularly to earlier-stage companies, helped fuel the rebound in R&D spending," the authors wrote. They note that 41 initial public offerings in the United States raised $3.3 billion that contributed to the boom.

Pharmaceutical companies increased their R&D budget in 2013 as well. In April, the pharmaceutical industry association PhRMA reported that its members spent $51.1 billion in 2013, up 3% from $49.6 billion in 2012. This change was driven by a 6.9% spending increase in the United States, versus a 9.1% decrease elsewhere.

PhRMA notes that in 2012 nearly 24% of its members' research spend was allocated to preclinical research. 8% went on Phase I trials, 11% went on Phase II trials, 32% went on Phase III trials, 8% went on approval, and the remaining 17% went on post-approval or uncategorized spending.

These numbers make for rosier reading for US-based researchers than did a recent analysis that looked at R&D spending only up until 2012. Justin Chakma, a venture capital investor at Thomas, McNerney & Partners in La Jolla, California, and his colleagues reported in January that inflation-adjusted biomedical spending in the United States fell between 2007 and 2012 while biomedical spending in Asia rose (*N. Engl. J. Med.* **370**, 3–6; 2014).

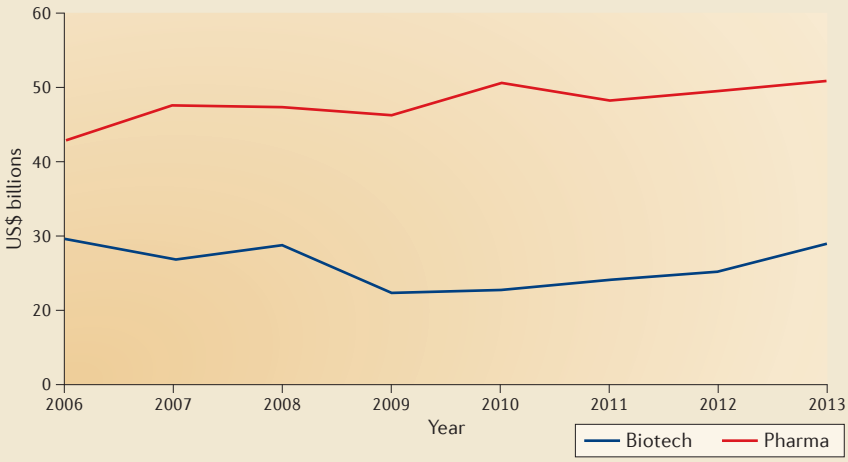


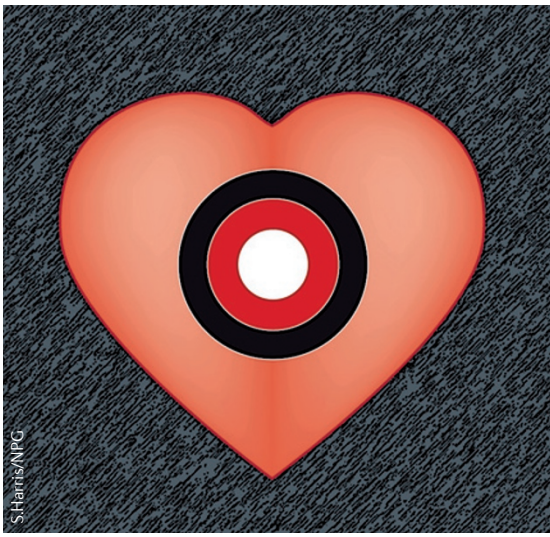
Figure 1 | **R&D spending from 2006 to 2013.** Biotech R&D spending data is from Ernst & Young Beyond Borders Global Biotechnology Report 2008, 2009, 2010, 2011, 2012, 2013 and 2014. Where annual reports provided inconsistent R&D spending data, data from latest report were used. Pharmaceutical R&D spending data are from PhRMA 2014 Profile. Some companies are included in both cohorts.

APOC3 joins genetically validated target list

Loss-of-function mutations in the *APOC3* gene are associated with reduced risk of coronary heart disease and ischaemic cardiovascular disease.

The lowdown: Two large-scale genetic validation studies have pointed the way to another putative cardiovascular target.

In a first study, members of the Exome Sequencing Project examined a cohort of 3,734 participants for mutations that were associated with low plasma triglyceride levels, a measure that has previously been



associated with reduced cardiovascular risk. Carriers of a rare *APOC3* mutation had plasma triglyceride levels that were 39% lower than those of non-carriers. When the researchers cross-validated the results by looking at the clinical importance of 4 loss-of-function *APOC3* mutations in 110,970 participants from 14 studies, they found that the 498 participants that were heterozygous for loss-of-function mutations had a 40% lower risk of coronary heart disease than did non-carriers (*N. Engl. J. Med.* **371**, 22–31; 2014).

In an independent study, Anders Berg Jørgensen from the University of Copenhagen, Denmark, and his colleagues found that loss-of-function *APOC3* mutations were associated with a 44% reduction in non-fasting levels of triglycerides. Clinical follow-up of participants showed that the incidences of ischaemic vascular disease and ischaemic heart disease were reduced in carriers by 41% and 36%, respectively (*N. Engl. J. Med.* **371**, 32–41; 2014).

"The results of our study highlight the potential usefulness of naturally occurring loss-of-function mutations in guiding the selection of therapeutic targets," write the members of the Exome Sequencing Project. They compare their findings to the discovery of loss-of-function mutations in the gene coding for proprotein convertase subtilisin kexin 9 (PCSK9), which sparked the development of a highly anticipated class of antibody therapies for hypercholesterolaemia (*Nature Rev. Drug Discov.* **11**, 817–819; 2012).

These data may be particularly important for Isis, which has an antisense APOC3 inhibitor in Phase II development for the treatment of elevated plasma triglycerides.