NEWS IN BRIEF

Industry R&D returns slip

The return on investment (ROI) for R&D is falling, say Deloitte analysts in their sixth annual report on the pharmaceutical industry's R&D performance. The analysis, based on data from a cohort of 12 life sciences companies, shows that the R&D ROI for these companies was down to 4.2% in 2015, from 10.1% in 2010 (see FIG. 1).

"Since 2010, the decline in the forecast peak sales of assets has had the greatest, negative impact on R&D returns," the authors write. They report that the average peak sales forecasts per asset has approximately halved, from US$816 million in 2010 to $416 million in 2015. "This reduction has been caused by multiple, distinct pressures from reimbursement, competition and smaller patient volumes," they write. An analysis of peak sales forecasts has shown, however, that these forecasts can be wildly inaccurate (*Nat. Rev. Drug Discov.* **12**, 737–738; 2013).

The Deloitte report also found that between 2010 and 2015 the average cost of developing an asset increased by around one-third, from $1.188 billion to $1.575 billion. A smaller 'extension' cohort of four mid- to large-cap companies fared considerably better on drug development costs, with an average development cost of $1.08 billion per asset. This extension cohort also outperformed the original 12 companies on every measure of R&D performance. "We believe this shows the economic viability of a different R&D business model which our original cohort could learn from," the Deloitte analysts write.

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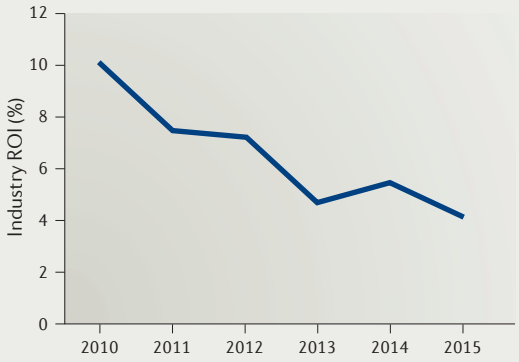

Figure 1 | **Industry R&D return on investment (ROI), as calculated in Deloitte's "Measuring the return from pharmaceutical innovation 2015".**

FDA approves drug from transgenic chicken

The FDA granted a first ever approval to a drug that is produced in the egg white of transgenically engineered chickens. The agency granted the green light to Alexion's enzyme replacement therapy sebelipase alfa for the treatment of a rare disease known as lysosomal acid lipase (LAL) deficiency or Wolman disease.

Chickens now join goats and rabbits in the pharmaceutical farm. In 2009, the FDA granted the first such approval to rEVO Biologics' antithrombin alfa, an anticoagulant that is produced in goat's milk and that was approved for various uses in hereditary antithrombin-deficient patients. Then, in 2014, the FDA approved Pharming's recombinant C1-esterase inhibitor, produced in rabbit's milk, for the treatment of hereditary angioedema.

At least three other drugs produced in transgenic animals are in development. TG Therapeutics is developing ublituximab, a CD20-targeting antibody, for the treatment of B cell proliferative disorders including non-Hodgkin lymphoma and chronic lymphocytic leukaemia. Its Phase III candidate, produced in the milk of modified goats, could be the first 'farmaceutical' antibody to make it to market.

rEVO's factor VIIa eptacog alfa, produced in the milk of transgenic rabbits, is in Phase III development for the treatment of haemophilia A and B. PharmAthene's organophosphorus scavenger protein pegylated butyrylcholin esterase, produced in the milk of transgenic goats, is in development for the prevention and treatment of nerve agent toxicity.

"The floodgates are opening and I can't wait to see what comes next," William Muir, a geneticist at Purdue University in West Lafayette, Indiana, told *Nature* on the news of the approval (*Nature*, published online 9 Dec 2015).

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Industry gets mixed transparency grades

Despite recent moves by the industry to provide access to clinical trial results, transparency rates vary widely between companies, found a recent study of clinical trial registration and reporting rates.

For a first attempt at setting up a transparency scorecard, Joseph Ross, of Yale School of Medicine, in Connecticut, and colleagues looked at trial registration and reporting rates for 15 drugs, sponsored by 10 large pharmaceutical companies and approved in 2012. On average, companies had only registered 57% of a drug's trials on ClinicalTrials.gov and had published or reported results of 65% of the trials (*BMJ Open* **5**, e009758; 2015). Two companies, GlaxoSmithKline and Johnson & Johnson, disclosed all the clinical trial results for all their approved drugs. Gilead, the lowest-scoring company, disclosed only 21% of the trial results for its anti-HIV combination of cobicistat, elvitegravir, emtricitabine and tenofovir.

The authors point to three reasons why legal disclosure requirements are not being met: stakeholders perceive the rules to be unclear and ambiguous; mergers and acquisitions, as well as collaborations and licensing agreements, can complicate responsibility for compliance; and a perceived lack of enforcement of the rules (the FDA can impose a penalty of $10,000 per day for lack of compliance, but never has).

The researchers now plan to generate a transparency scorecard and ranking system for all newly approved drugs to "motivate and increase transparency, thereby supporting existing transparency initiatives, advancing clinical innovation, promoting a trustworthy innovation sector and strengthening protection of human research subjects globally".

A separate analysis by the health publication *STAT* found that many academic research institutes are also failing to meet reporting requirements, violating federal reporting rules. Stanford University, the University of Pennsylvania, the University of Pittsburgh and the University of California, San Diego — four of the top 10 recipients of federal medical research funding — disclosed research results late or didn't disclose them at all at least 95% of the time since reporting became mandatory in 2008.

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