NEWS IN BRIEF

R&D returns continue to fall

Big pharma's return on investment for R&D expenditure fell to 3.7% in 2016, shows an annual report from Deloitte (FIG. 1). This marks a low point since the consultants started tracking these data in 2010.

The analysis tracks the R&D returns of 12 large pharma companies: Amgen, AstraZeneca, Bristol-Myers Squibb, Eli Lilly, GlaxoSmithKline, Johnson & Johnson, Merck & Co., Novartis, Pfizer, Roche, Sanofi and Takeda. There was considerable variability within the returns of the cohort. Three companies achieved returns of more than 7%, and six companies fared better in 2016 than in 2015.

The report notes that revenue is increasingly coming from 'self-originated' assets that are developed in house: 58% of forecast revenue from the late-stage pipeline is from self-originated projects in 2016, up from 39% in 2013. This trend, combined with the falling returns, suggests that "companies are struggling to replace pipeline value through self-originated assets," the authors write.

"We anticipate that the coming years will see increasing [merger and acquisition] activity in a quest for higher R&D returns through R&D cost synergies or the acquisition of valuable assets," the authors write. This kind of remedy, however, can have a high financial, organizational and scientific price.

The report also notes that the average cost of moving an agent from discovery to launch stabilized for companies in this cohort, at just over US$1.5 billion. Last year, Joseph DiMasi, of Tufts University, Medford, Massachusetts, USA, and his colleagues used a different methodology from a different cohort of companies to calculate the cost of drug development at $1.4 billion. When they included the opportunity cost of drug development, the expense rose to $2.6 billion.

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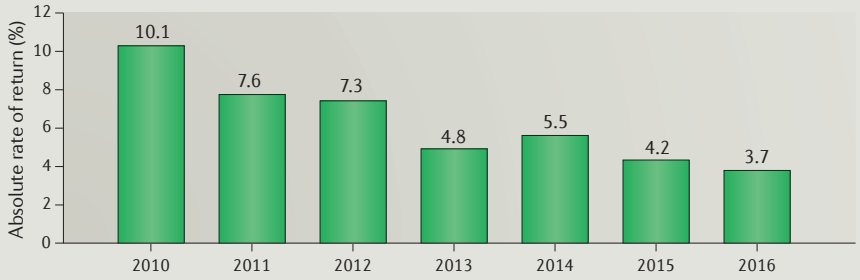

Figure 1 | **R&D returns on investment.** Source: Deloitte LLP.

Cures Act shakes up the FDA and NIH

President Barack Obama signed the 312-page 21st Century Cures Act into law, bringing sweeping changes to both the FDA and NIH.

One of the broadest changes in the Act is that the FDA must work to incorporate real world data into its regulatory decision-making processes. The Act defines real world data loosely as data from sources other than randomized clinical trials, and notes that they include safety surveillance studies, observational studies and registries. It directs the agency to establish a draft framework for the use of real-world data within 2 years.

Last month, the FDA cautioned in the *New England Journal of Medicine* that real world data have to be handled with care. "The confluence of large data sets of uncertain quality and provenance, the facile analytic tools that can be used by non-experts, and a shortage of researchers with adequate methodologic savvy could result in poorly conceived study and analytic designs that generate incorrect or unreliable conclusions," it wrote. "Caution is still needed, and expectations of 'quick wins' resulting from the use of such evidence should be tempered accordingly."

The Cures Act also introduces a new pathway for the approval of antibiotic drugs for small populations. The so-called 'limited population pathway' provides a means to approve antibacterial agents for serious and life-threatening infections in limited patient populations on the basis of a favourable benefit–risk profile. The agency has 18 months to issue draft guidance describing criteria, processes and other general considerations for demonstrating safety and efficacy under this new pathway.

The Cures Act also creates a new designation called 'regenerative advanced therapies'. This designation is reserved for stem cell therapeutics and related approaches that have clinical data showing a potential to address unmet need for serious or life-threatening conditions. It will provide benefits in line with the Breakthrough Drug designation, enabling closer cooperation between regulators and drug developers to expedite drug development.

Some groups wanted even faster approval pathways for regenerative medicines. But the FDA pushed back. "We believe that the assertion that existing standards for regulatory approval are too rigorous for stem-cell therapies results largely from a lack of familiarity with the available pathways for developing cellular therapy products and from the lack of a systematic, facilitated approach to assembling the clinical data necessary to support the licensure of stem-cell therapies produced by individual practitioners at different sites. For serious and life-threatening diseases in which there is unmet medical need, expedited pathways are readily available," it recently wrote in another article in the *New England Journal of Medicine*.

Other provisions in the Act include measures that aim to bolster: patient-focused drug development; the qualification of drug development tools; the oversight of continuous manufacturing of pharmaceuticals; and the development of novel clinical trial designs. The Act also raises the salary cap for FDA jobs, to facilitate the hiring and retention of staff.

The FDA is now negotiating the terms of Prescription Drug User Fee Act (PDUFA) VI with industry stakeholders, and could receive a new commissioner under President-Elect Donald Trump, which could lead to further changes at the agency in 2017.

At the NIH, changes under the Cures Act include the authorization of US$4.8 billion over 10 years in extra funding. This is less than the $8.8 billion envisioned by earlier versions of the Bill. Some critics are also concerned that the majority of new funding is directed to large top-down big science projects, rather than investigator-initiated grants. The Cancer Moonshot will get $1.8 billion, The Precision Medicine initiative will get $1.5 billion and Brain Research through Advancing Innovative Neurotechnologies (BRAIN) initiative will get $1.5 billion.

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