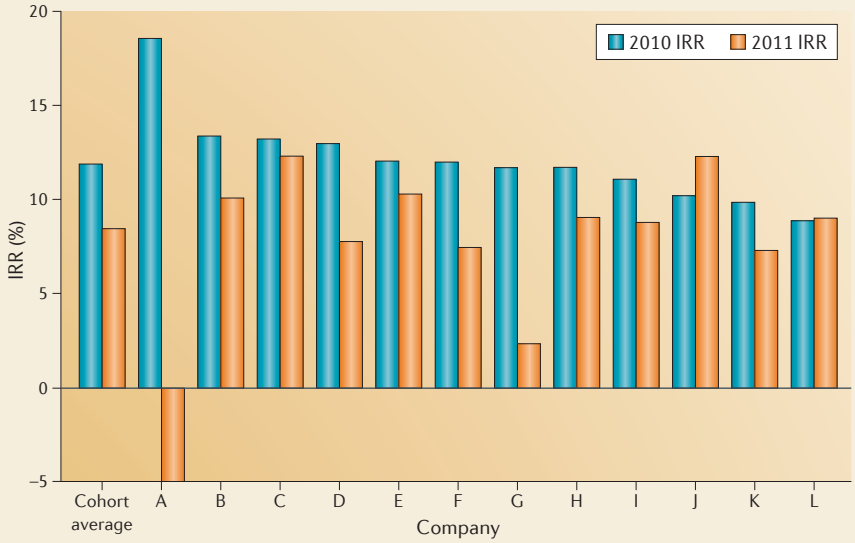
NEWS IN BRIEF

Falling R&D returns?

The internal rate of return for R&D has fallen on average from 11.8% in 2010 to 8.4% in 2011, finds a joint analysis by Deloitte and Thomson Reuters.

The lowdown: An annual review by Deloitte and Thomson Reuters set out to assess returns on research and development (R&D) for a cohort of the top research-based pharmaceutical companies, measured by R&D spending in 2008–2009. Internal rate of return (IRR) — which, for a good investment, should be higher than the cost of capital — has fallen in 10 out of 12 members, on average by 30% (see figure). In part, they add, this is because the cost of bringing new drugs to market has increased. "The average cost of capital for these companies is probably on a par with average R&D IRR," estimates Deloitte analyst Julian Remnant. The cohort consists of: Pfizer, Roche, Novartis, Sanofi, GlaxoSmithKline, Johnson & Johnson, AstraZeneca, Merck & Co., Eli Lilly, Bristol-Myers Squibb, Takeda and Amgen.



Source: Deloitte and Thomson Reuters research.

Amgen springs Enbrel patent surprise

Amgen has received an additional 17 years of patent protection for its blockbuster immunosuppressant etanercept (Enbrel), even as competitors readied biosimilar competition.

The lowdown: Etanercept, a fusion protein that inhibits tumour necrosis factor signalling, was approved for the treatment of rheumatoid arthritis in 1998 — the first of several approvals for autoimmune diseases — and has become a key product for Amgen and Pfizer, with worldwide sales of over US$6 billion in 2010. With its patent protection anticipated to expire in October 2012, companies including Merck & Co. had publicly disclosed plans to develop competing biosimilars. In November, however, Amgen unexpectedly announced that a newly granted US patent (US 8,063,182) will extend the product's patent protection until 2028.

According to current US law, patents receive a term of 20 years from their earliest US filing date. But Amgen's newly granted patent was filed in May 1995, one month before the current standards were introduced, and so it instead receives a term of 17 years from the date of grant. The initial filing also preceded a 1999 change in US law that requires the US Patent and Trademark Office to publish most pending patent applications — introduced to prevent so-called 'submarine' patents that take competitors by surprise. A timeline of the review process for the new patent shows that it was lost internally for 2 years at the US Patent and Trademark Office, but otherwise bounced regularly back and forth between the reviewers and the claimant.

"Patents that are entitled to a 17-year term from issuance are now rare, and will become increasingly more so," says Dan Becker, a patent attorney at Dechert. "There cannot be very many applications still pending in the Patent Office that were filed before June 1995." Beginning next September, a new procedure made available by the recently enacted patent reform legislation — inter partes review — may provide an opportunity for competitors to challenge the patent, he adds.

Integrating whole-genome sequencing into drug trials

A pilot study has highlighted the possibility, and the challenges, of using whole-genome sequencing to stratify patients into oncology clinical trials.

The lowdown: Oncology clinical trials are increasing using genomic information to enrol patients, but tend to only assess the status of a few specific genes of interest. To explore the feasibility of instead using a whole-genome sequencing approach to stratify patients, Sameek Roychowdhury, of the University of Michigan, USA, and his colleagues set up a pilot trial (*Sci. Transl. Med.* **3**, 111ra121; 2011). In one stage of the trial, biopsy samples were taken from tumours of two patients with advanced or refractory cancer and assessed using whole-genome sequencing; results were then discussed by a multidisciplinary team. Both patients were identified as possible candidates for treatment with phosphoinositide 3-kinase inhibitors, cyclin-dependent kinase inhibitors or BRAF plus MEK inhibitors. There were, however, no suitable trials to enrol either patient into, highlighting a key hurdle for the personalized oncology approach: "You have to have a lot of trials planned, and drugs available upfront, to be able to do this successfully," says Roychowdhury.

For the pilot study a predetermined list of potentially informative genes was used to filter the results and facilitate evaluation, but the full value of whole-genome sequencing may lie in its ability to advance research agendas, says Roychowdhury. A comparison of the tumour genomes of patients before they are enrolled in a trial and after they have relapsed, for instance, could enable a better understanding of the mechanisms of drug resistance and help oncologists design drug combinations upfront that will better delay disease progression.

The cost of sequencing (US$3600) was not prohibitive, and nor was the time needed to sequence the whole genome (4 weeks), he adds. "Within a year or two, the cost, the time to complete sequencing, all the technological hurdles will get easier."