NEWS IN BRIEF

Rare disease bonanza

The European Commission committed €144 million to 26 rare disease research projects.

The lowdown: The European Commission announced the rare disease research funding, which will go to over 300 research participants from 29 European countries, on Rare Disease Day. The projects cover a broad spectrum of rare diseases — including cardiovascular, metabolic and immunological disorders — and will focus on improving the understanding, diagnosis and treatment of disease. Seventeen projects received more than €5 million in funding. The top funded projects are shown in the table below; a full list is available online at go.nature.com/eUJ4eC.

Many of these new projects will contribute to the International Rare Diseases Research Consortium (IRDiRC), a collective that aims to deliver 200 new therapies by 2020.

Rare disease project	Funding (million)
Neuromics: integrated European omics research project for diagnosis and therapy in rare neuromuscular and neurodegenerative diseases	€12
RD-CONNECT: an integrated platform connecting registries, biobanks and clinical bioinformatics for rare disease research	€12
EURenOmics: European Consortium for high-throughput research in rare kidney diseases	€12
BALANCE: development of a bioartificial liver therapy in acute liver failure	€6
DevelopAKUre: clinical development of nitisinone for alkaptonuria	€6
FIGHT-HLH: first targeted therapy to fight hemophagocytic lymphohistiocytosis	€6
GAPVAC: glioma actively personalized vaccine consortium	€6
MeuSIX: clinical trial of gene therapy for mucopolysaccharidosis type VI — a severe lysosomal storage disorder	€6
Net4CGD: gene therapy for X-linked chronic granulomatous disease	€6
PREVENTROP: new approach to treatment of the blinding disease retinopathy of prematurity	€6
PROFNAIT: development of a prophylactic treatment for the prevention of fetal/neonatal alloimmune thrombocytopaenia	€6
Traumakine: interferon-beta treatment of acute respiratory distress syndrome	€6

Eye on ibrutinib

The FDA granted 'breakthrough' designation to the BTK inhibitor, helping Pharmacyclics raise US$207 million through the sale of shares.

The lowdown: Bruton's tyrosine kinase (BTK), a key mediator of B cell development with minimal effects outside the B cell lineage, has attracted attention as a target for lymphoid malignancies (*Nature Rev. Drug Discov.* **12**, 229–243; 2013). Leading the pack is Pharmacyclics and Johnson & Johnson (J&J)'s Phase III candidate ibrutinib.

In February, the covalent inhibitor got a boost when the US Food and Drug Administration (FDA) awarded the drug the 'breakthrough' designation, the agency's newest pathway for expedited drug development. The designation will support development for two B cell malignancies: relapsed or refractory mantle cell lymphoma (MCL) in patients who have received prior therapy, and Waldenström's macroglobulinaemia. Neither J&J nor Pharmacyclics would disclose the implications of the breakthrough designation for their development strategy, but the news nevertheless fuelled a $207 million share offering from Pharmacyclics in March. The company says it will use the proceeds to "accelerate commercial readiness" of its candidate.

J&J and Pharmacyclics are running five Phase III trials of the first-in-class agent and expect to file for approval in the MCL indication by the end of the year. Analysts hope the drug will eventually find use in larger haematological cancer indications as well, such as diffuse large B cell lymphoma, follicular lymphoma and multiple myeloma. Analysts forecast annual sales of $1.5 billion for the drug by 2017, according to Thomson Reuters Cortellis.

The other selective covalent BTK inhibitors in clinical development are Celgene's CC-292 and Ono's ONO-4059. Both are in Phase I trials. Bristol-Myers Squibb's multikinase inhibitor dasatinib, which is approved for chronic myeloid leukaemia and acute lymphoblastic leukaemia, has activity against BTK as well as BCR–ABL and SRC proteins.

Resolving sirtuin uncertainty?

Sirtuin-activating compounds act directly on SIRT1 via an allosteric mechanism, suggests the latest salvo in the sirtuin story.

The lowdown: Sirtuins have been making waves since well before GlaxoSmithKline (GSK) paid US$720 million to acquire Sirtris and its pipeline of resveratrol and synthetic sirtuin 1 (SIRT1) activators in 2008. Proponents argue that these 'anti-ageing' agonists could become blockbusters in a range of indications, while critics say that the SIRT1 activity signal elicited by Sirtris's compounds is an assay artefact. Several groups, including Amgen and Pfizer, have questioned the fluorescent readout of SIRT1 activity assays and have concluded that resveratrol and related compounds are not direct activators of SIRT1 (*Chem. Biol. Drug Des.* **74**, 619–624; 2009; *J. Biol. Chem.* **285**, 8340–8351; 2010).

David Sinclair, a molecular biologist at Harvard Medical School in Boston, Massachusetts, USA, and co-founder of Sirtris, and his colleagues have now honed their SIRT1 assay and revisited the activity of these compounds. "SIRT1 can be directly activated through an allosteric mechanism common to chemically diverse [sirtuin-activating compounds]," they write, after running the assay with different SIRT1 substrates and SIRT1 mutants (*Science* **339**, 1216–1219; 2013).

"This paper demonstrates that you can effectively reproduce data that had been published before with a faulty assay," says Raphael de Cabo, a molecular biologist at the Laboratory of Experimental Gerontology in Baltimore, Maryland, USA, who was not involved in the study. "The question that remains open is whether the activity of these compounds is solely dependent on SIRT1," he adds. The findings and the new assay could open the door to the development of SIRT1-specific agents.

GSK halted development of its once-lead SIRT1 activator resveratrol in 2010, but continues to work on GSK-2245840 (SRT2104), which has been tested in Phase II trials for psoriasis and Phase I trials for ulcerative colitis. Sirtris had operated as a stand-alone GSK unit in Cambridge, Massachusetts, until last month, when the pharma announced it was consolidating Sirtris's laboratories into GSK facilities in Philadelphia, Pennsylvania.