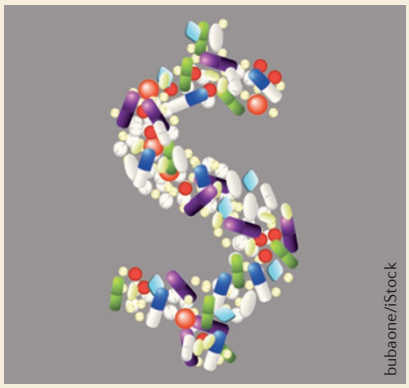
NEWS IN BRIEF

AbbVie pays $21 billion for Pharmacyclics' BTK inhibitor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When the US Food and Drug Administration approved Pharmacyclics' Bruton tyrosine kinase (BTK) inhibitor ibrutinib in November 2013, just 3 short years after it had entered into clinical testing, it was clear the small molecule was destined for a big future. AbbVie's purchase of Pharmacyclics for US$21 billion — providing rights to just one-half of the sales from the drug, which Pharmacyclics splits with Johnson & Johnson — shows that expectations for the first-in-class BTK inhibitor are still sky-high.

The drug is currently only approved for chronic lymphocytic leukaemia and for two rare blood cancers. But mid- and late-stage trials are testing the drug in other potentially profitable oncology indications, including non-Hodgkin lymphomas, multiple myeloma and acute myelogenous leukaemia. AbbVie aims to explore combinations to further expand ibrutinib's reach, potentially including the combination of ibrutinib plus AbbVie's Phase III B-cell lymphoma 2 (BCL-2) inhibitor, ABT-199 (go.nature.com/71T9kS). The BTK inhibitor may also act synergistically with immunotherapeutics to offer efficacy in solid cancers like breast cancer (*Proc. Natl Acad. Sci. USA* **112**, E966–E972; 2015).

A few other companies are also developing BTK inhibitors for oncology indications. Acerta's ACP-196 is in Phase II trials for pancreatic cancer and in Phase I/II trials for lymphomas. Celgene's CC-292 is in Phase I trials for lymphomas. Gilead's GS-4059 is in Phase I trials for haematologic cancers.

Beyond oncology, Acerta and Celgene are developing their BTK inhibitors for rheumatoid arthritis (in Phase II trials). Pharmacyclics also has an ongoing trial of ibrutinib in a Phase I/II trial for graft-versus-host disease, and Merck KGaA has a BTK inhibitor in Phase I trials for autoimmune disorders.

Pharmacyclics also has a histone deacetylase (HDAC) inhibitor (see also *Nature Rev. Drug Discov.* **14**, 225–226; 2015) and a factor VIIa inhibitor in Phase I/II oncology trials.

Asher Mullard

Industry head-to-head trials favour sponsor

With payers increasingly pushing back against high drug prices, head-to-head trials provide one way to prove the value of a new drug. An analysis by Stanford's John Ioannidis and colleagues now shows, however, that not all head-to-head trials are created equal. Key differences in trial design by industry and non-profit organizations may underlie differences in trial outcomes, they report (*J. Clin. Epidemiol.* 7 Feb 2015 [epub ahead of print]).

Ioannidis and colleagues analysed 319 head-to-head trials that were published in 2011, 182 (57%) of which were sponsored by industry. They found that 83% of the industry-sponsored trials yielded 'favourable' results for the trial sponsor, compared with 58% for trials sponsored by non-profit organizations. Industry groups were also more likely to use a non-inferiority design (29%) than were non-profit groups (18%). Industry funding and the use of non-inferiority designs were both strongly associated with trials that returned 'favourable' findings for their sponsors.

Industry-sponsored trials were also, on average, nearly twice as large as non-profit sponsored trials, although trial size was not associated with 'favourable' findings.

The authors suggest four possible reasons for why industry's head-to-head trials may be more likely to yield favourable results: industry may conduct trials "more rigorously … and are thus genuinely more successful"; industry may "selectively fund trials that are more likely to yield favorable results"; industry may "choose suboptimal outcomes, comparators, and other design features that can secure a favorable result"; or "trials with unfavorable findings may be less likely to be published by companies". "Given the importance of head-to-head comparisons in informing guideline recommendations and practice, consideration should be given to allowing the conduct of more large trials of comparative effectiveness and safety under the control of nonprofit entities," the authors conclude.

Asher Mullard

Oral GLP1 analogue rounds Phase II corner

Novo Nordisk's oral formulation of semaglutide met its primary end point in a Phase II trial, suggesting changes could be coming for the increasingly crowded antidiabetic glucagon-like peptide 1 (GLP1) drug class.

The US Food and Drug Administration approved AstraZeneca's first-in-class GLP1 analogue exenatide for type 2 diabetes in 2005. The class has since grown with the approval of once-daily and once-weekly formulations of the therapies, which enhance insulin secretion. The market for GLP1-receptor agonists was worth US$3 billion in 2014, and is set to grow to $9 billion by 2023, according to Decision Resources. Novo Nordisk now seems to have cracked the oral delivery of these peptide therapeutics, and hopes it may be able to grow and dominate the market with an oral formulation of semaglutide. The company is also developing a once-weekly subcutaneous formulation of semaglutide.

In the 600-patient Phase II trial, glycated haemoglobin (HbA1c) levels improved by 0.7–1.9% in patients treated with different doses of the oral GLP1 analogue. HbA1c levels improved by 1.9% in a subcutaneous semaglutide comparator arm, and by 0.3% in a placebo comparator arm. Weight loss with the highest oral dose of semaglutide was comparable to weight loss with injected semaglutide.

Novo Nordisk is now considering its options for Phase III trials of their oral antidiabetic. The data suggest, however, that they may need 300-fold the amount of active ingredient to succeed with their oral drug (it is dosed at 40 mg per day for oral treatment, versus 1 mg per week for subcutaneous treatment), leading to some concerns about the commercial viability of this oral approach.

TransTech Pharma also has an oral GLP1 agonist in Phase II trials. Its TTP054 is a small molecule, however, rather than a peptide.

Intarcia, meanwhile, is developing a matchstick-sized device that is inserted under the skin to slowly release exenatide over 6 or 12 months. Their device has already cleared two Phase III trials (*Nature Biotech.* **32**, 1178; 2014).

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