IDX184, unlike BMS-986094, is not based on phosphoramidate chemistry. BMS-986094 gives rise to methoxy, naphthol and neopentyl metabolites. "At least in our hands all three of those modifications lead to increased cytotoxicity in cells," claims Mayers. Yet the most advanced nucleoside in development for HCV infection, Gilead's GS-7977 (formerly PSI-7977), is also a phosphoramidate and shares a structural motif with BMS-986094, although it includes a uridine rather than a guanosine base. Elsewhere, Edinburgh, UK–based NuCana BioMed is applying McGuigan's phosphoramidate technology to improve the delivery of cancer drugs, beginning with the nucleoside analog gemcitabine. Its plans to start clinical trials around now have not been affected by the BMS trial, says CEO Hugh Griffith.

The common thread linking the present trial and other less serious setbacks in nucleoside drug development has been the presence of a guanosine base. "It's not a tried and tested nucleoside, or nucleotide for that matter," says Griffith. Development of IDX184 was temporarily halted in September 2010, when liver damage occurred in three healthy volunteers undergoing a drug-drug interaction study involving IDX184 and IDX320, a protease inhibitor that has since been dropped. Pharmasset halted development of PSI-938, a cyclic phosphate prodrug of β-D-2'-deoxy-2'-α-fluoro-2'-β-C-methylguanosine-5'-monophosphate (*Antimicrob. Agents Chemother.* **56**, 3767–3775, 2012), just before its $11-billion sale to Gilead in early 2012, when liver abnormalities were seen in a combination trial with GS-7977.

The emergence of cardiotoxicity is, however, a new and far more devastating development, and the outlook for several of the surviving patients is not good. One now needs a heart transplant. "Others are deteriorating," says Stephen Sheller, of the Philadelphia law firm Sheller PC. In that context, the presentation last June by UK science minister David Willetts of a business innovation award to celebrate the "impact" of McGuigan's continuing partnership with BMS looks tragically premature.

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Deals center on self-reported patient data services

Two announcements made over the summer indicate an increasing interest in tapping into online services that collate self-reported clinical data. Merck entered a collaboration with the social networking health site PatientsLikeMe of Cambridge, Massachusetts, to use members' information as a proxy for clinical data. One month earlier, direct-to-consumer genetic information provider 23andMe acquired Cure Together, a Canadian enterprise originating at the University of Toronto that brings together patients sharing self-reported symptoms.

PatientsLikeMe allows individuals with a medical condition to interact, share their stories, and—most interestingly for research—compare medications, symptoms, disease progression and adverse events to drugs. Merck is tapping into the PatientsLikeMe psoriasis community, which is currently some 2,000 strong, to help evaluate the impact of the disease and its current treatments. Clinical researchers and epidemiologists at the Whitehouse Station, New Jersey–based pharma will gain access to the community's health profiles, forum postings and journal entries in hopes that the data will help "uncover insights about the disease that may lead to better approaches for patients managing their condition day to day, providers creating care plans and researchers developing treatments," says PatientsLikeMe co-founder Ben Heywood.

Website users embrace the company's data-sharing policy. "We believe sharing your healthcare experiences and outcomes is good. Why? Because when patients share real-world data, collaboration on a global scale becomes possible," the website states.

PatientsLikeMe has already been used to invalidate claims made from small-scale efficacy trials of off-label uses of existing approved treatments. For example, a 2008 Italian study in *PNAS* (**105**, 2052–2057, 2008) suggested that lithium—a drug approved for bipolar disorder—could also slow the progression of amyotrophic lateral sclerosis (ALS). Hundreds of members of PatientsLikeMe began taking the drug and reporting their results over a 12-month period through the site; an algorithm to match cases to controls was then used to conduct a patient-led observational study. The online results reported by participating patients did not support the earlier claims (*Nat. Biotechnol.* **29**, 411–414, 2011).

Since that validation study, several companies have been working with PatientsLikeMe to explore ways in which self-reported patient data can support internal decision making in drug programs or facilitate recruitment in trials. For example, Novartis of Basel described its previous partnership on multiple sclerosis and transplantation with the site as "helpful to gain increased knowledge of patients' insights on their disease and their journey, so that as a company we could support patients as an informed partner." A partnership between Avanir Pharmaceuticals of Aliso Viejo, California, and PatientsLikeMe to survey amyotrophic lateral sclerosis patients and inform them of an upcoming trial, resulted in a fully enrolled clinical trial, according to Randall Kaye, Avanir's chief medical officer.

PatientsLikeMe co-founder Ben Heywood.

The PatientsLikeMe website currently lists 11 biopharma collaborators. Companies pay for access to the data and their fees, in turn, fund PatientsLikeMe's own data mining and research.

Another company seeking to liaise directly with patients and their data to spur biomedical research is 23andMe. The Mountain View, California–based company's main product assays more than one million single-nucleotide polymorphisms for a fee; the company then invites its customers to contribute their genetic data alongside their self-reported phenotypic information on the 23andMe website and is interested in mining the information for research questions.

In mid-July, 23andMe took a further step with the acquisition of Cure Together, a crowdsourcing enterprise. In this community platform, patients exchange experiences on the impact of prescription drugs on over 600 medical conditions across 110 countries. Though the company has not yet announced any outside research collaborations making use of the Cure Together community, the acquisition "will improve our own ability to gather data for research and give customers more tools to explore and participate in online communities," 23andMe announced on its blog.

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