uncertain over what to expect from Gilead. The US biotech was undergoing a change of leadership—O'Day started on March 1 of this year—and its plans were unclear. At the time, however, “there was no concrete acquisition offer from Gilead, or from anyone else.”

Gilead could have approached Galapagos's major shareholders directly with an acquisition offer, bypassing the CEO. (Those shareholders include a Rotterdam, Netherlands-based family office, Van Herk Investments, which was also one of the largest holders of Ablynx stock and, despite being a self-declared long-term investor, happily accepted the 100% premium offered by Sanofi.) But they did not. “When a company is successful, it is difficult [for the potential acquirer] to go hostile,” says Geoffrey Porges, director of therapeutics research and a senior research analyst at SVB Leerink. Buying a company against management's wishes, by seeking shareholders' approval directly, spoils the creative culture that often underpins much of the deal's value, sending founders and loyal scientists fleeing. That scenario would not serve Gilead, under pressure to deploy its \$30 billion cash pile (courtesy of its legacy hepatitis C virus drug franchise and an expanding HIV therapy portfolio) to enhance the pipeline. “It takes time to build a productive drug discovery platform,” says O'Day, acknowledging the need for both the technology and Galapagos scientists' know-how in applying it. “This [deal] is a major step forward for Gilead's portfolio. It doubles our research base and significantly increases our IP, expertise and capabilities in fibrosis,” he said on a 14 July conference call.

This deal was designed so that Gilead could tap into its smaller partner's innovation without squashing it and shows how all pharma and biotech should work together, according to van de Stolpe. The tie-up shares some similarities with both Roche-Genentech and Sanofi's 2015 immuno-oncology partnership with Regeneron, both of which “involved cash for research, equity, board seats and defined terms for future development and commercialization,” says Porges. (This year, Sanofi and Regeneron narrowed down their collaboration around two clinical-stage assets.) Whether the Gilead-Galapagos variation proves inspirational to pharma or biotech in the future will depend on how many of Galapagos's drug candidates actually succeed. If just one does, Gilead may have overpaid. If several do, the US company has gotten a great deal and Galapagos's shareholders may feel they were sold short.

Granted, the deal removes the risk of an unwanted acquisition, meets Galapagos's fundraising needs for the next ten years, and puts a floor under its share price. But

it also caps that share price by snuffing out any upside from merger speculation. The European biotech has also relinquished valuable US rights to any drugs that do succeed and will bear increased development costs. Some observers also question how independent the biotech will really be because the new deal gives Gilead two members on the board who could “potentially veto anything they don't like,” cautions one former biotech CEO, who suggests the deal is “an acquisition in all but name.”

The deal may not be a slam dunk for Gilead, either. Galapagos's R&D engine has been productive so far, but has yet to generate a marketed drug. Filgotinib will probably be approved, perhaps as a safer alternative to existing JAK inhibitors like Eli Lilly's Olumiant (baricitinib) and Pfizer's Xeljanz (tofacitinib), which come with serious side-effects. (The higher dose of Xeljanz received a boxed warning in ulcerative colitis in late July 2019). But following late into a very crowded, big-pharma-dominated rheumatoid arthritis market will not be easy, either in the United States or Europe, where cheaper biosimilars of AbbVie's best-selling Humira (adalimumab) are starting to push down prices. “The investment community does not share Gilead's confidence in filgotinib,” says Porges. And it is unlikely that both the IPF and osteoarthritis development candidates hit the jackpot.

O'Day is looking beyond these two candidates, though. He's eyeing the almost two dozen preclinical assets, including some that appear to both stimulate anti-inflammatory cytokines and inhibit pro-inflammatory cytokines. “One or two compounds per year could come into the clinic—or more, given increased funding. I am at peace if [the] osteoarthritis and IPF [candidates] don't hit. You have to be long-term minded when approaching discovery research,” says O'Day. Van de Stolpe insists that oncology remains off the table because the company's discovery platform, using primary human cells rather than cell lines, provides insufficient competitive edge in this indication.

For now, Gilead has a tight, but friendly, hold on Galapagos in a deal structure that has many positives for both sides. Yet “you never know how things go. If the market economics make sense for Gilead to buy [Galapagos], even a stand-still agreement is still negotiable,” says Dharminder Chahal, investment manager at Van Herk Investments.

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New antibodies best ZMapp in Ebola trial

Two antibody therapies for Ebola have performed well in a late-stage clinical trial being conducted during the Ebola outbreak in the Democratic Republic of the Congo. The study, called PALM (an abbreviation for a Swahili phrase meaning “together save lives”) was testing Regeneron's REGN-EB3, a collection of three fully human monoclonal antibodies; Ridgeback Biotherapeutics single monoclonal antibody mAb114; the nucleotide-analog antiviral remdesivir, developed by Gilead Sciences; and Mapp Biopharmaceutical's ZMapp, a cocktail of monoclonal antibodies against Ebola glycoproteins. ZMapp, the only candidate drug previously studied in Ebola patients, was being used as the control arm in PALM because it showed a favorable survival trend in an earlier trial. Following an August review, an independent data and safety monitoring board (DSMB) stopped the trial of the four therapies, recommending that participants now be randomized to receive only REGN-EB3 or mAb114. The preliminary PALM data showed a 29% mortality rate for participants treated with REGN-EB3 and 34% with mAb114, versus 53% with remdesivir and 49% with ZMapp.

“It was clear to the DSMB that those agents are more effective than the other two,” NIAID director Anthony Fauci said in an audio briefing. “Today, we have taken new steps. From now on, we will no longer say that EBOV is not curable,” added PALM principal investigator Jean-Jacques Muyembe-Tamfum.

A week before the PALM trial announcement, the Sabin Vaccine Institute licensed rights to three vaccine candidates, including a phase 2 vaccine against Ebola, from GlaxoSmithKline.

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“Although none of our companies are working on germline therapy, when I talk to people not involved in the biotechnology business, one of the first questions I get is: ‘Aren't you worried about designer babies?’ I am spending more time on this kind of question than at any point in my career.” Jim Burns, CEO of Casebia and cochair of the Alliance for Regenerative Medicine task force on gene editing. The group put out a statement in August that germline gene editing is currently inappropriate. (Financial Times, 26 August 2019)