IN brief

GSK's Harvard cash injection

Stem cell research at the Melton lab, Harvard University.

GlaxoSmithKline (GSK) and Harvard University have signed a 5-year, \$25 million research agreement to study stem cells. The landmark alliance delivers a boost for stem cell research, and is especially noteworthy coming from big pharma. The London-based company will fund

research at the Cambridge, Massachusetts-based Harvard Stem Cell Institute (HSCI) and Harvard Medical School-affiliated hospitals, as well as support annual early-stage research grants and staff exchange programs. The collaboration will be managed by a joint steering committee, and will focus its efforts primarily on improving drug screening technologies. "We can see a change in attitudes on both sides as academia and companies perceive that we need each other, but this doesn't mean that basic research will lose its independence," says Brock Reeve, executive director at HSCI, who also comments, "This joint venture will generate shared rights as both partners will put IP [intellectual property] on the table." GSK is not the only big drug company getting cozy with academia. New York-based Pfizer, Novartis of Basel and London's AstraZeneca have all signed agreements in the past with the likes of the University of California in San Francisco, the Massachusetts Institute of Technology and Washington University in St. Louis. Deals between industry and academia seem to be on the rise, but this collaboration is a first for stem cells, a sign that the field is maturing or of stem cells' increasing currency as a tool for pharmaceutical discovery. Only two weeks after the announcement, researchers from the Children's Hospital Boston, Massachusetts General Hospital, Harvard Medical School and Washington University published 20 disease-specific induced pluripotent stem cell lines (*Cell*, published online, doi:10.1016/j.cell.2008.07.041, 7 August 2008). The cells derived from people with hereditary disorders could provide cell lines for drug testing and eventually help reengineer disease-free cells for therapy. Corey Goodman, president of Pfizer's Biotherapeutics and Bioinnovation Center, an outsider to the deal, also perceives a change in attitudes. "The principle is that barriers are coming down, as both pharma and academia find new ways to partner and move innovative discoveries across the goal line. It's not so much about the money put in these collaborations but the tremendous opportunity that it provides for patients worldwide, at a time when most venture capitalists are changing their investment model." Pfizer created its own regenerative medicine unit last April in Cambridge, UK, and Cambridge, Massachusetts. —Victor Alamo-Bethencourt

Box 1 The price is right?

Roche's offer of \$89 a share (\$43.7 billion in total) is an 8.8% premium to Genentech's trading price the day before the announcement was made. Genentech has not been particularly enthusiastic in response. After three days of silence, it first said only that it would form a special committee of its board to determine its next move, noting that there was "no assurance that the special committee will approve any transaction with Roche." Genentech had total operating revenues of \$11.7 billion last year and boasts a deep pipeline. Knowing this, the response to the offer from observers has been universal: too little. After meeting privately for two weeks the special committee emerged to declare the offer inadequate—but, in a move that leans toward finding common ground, suggested it would consider a higher bid. (As of press time, Genentech's shares have traded up to more than \$99, reaching a new 52-week high.) Built into the companies' affiliation agreement is a stipulation that if the majority of the minority shareholders do not vote for the Roche takeover, the price will be determined by the average of estimates put forth by two independent investment banks. Genentech has suggested it can fight that clause, and attorneys for minority shareholders have asked a Delaware court to invalidate the affiliation agreement. Roche remains confident the acquisition will happen, and most observers tend to agree, but at a higher price. Lehman Brothers, in New York, suggests the price will reach \$105 per share, with an agreement in place by late October. Katherine Kim expects it will require between \$100 and \$110 per share to get the deal done.

BMS is offering \$60 per share (\$4.5 billion in total) to acquire the 83% of ImClone it doesn't already own. Here, too, investors have bid up the stock following the initial offer—it has traded at >\$65. After the bid, ImClone responded that the offer "greatly undervalues" the company, and Chairman Carl Icahn says ImClone had been considering splitting the company into two units, one focused on Erbitux and one for the pipeline. He has also insinuated that another board member (a BMS employee) might have disclosed these plans to BMS. No matter, outsiders suggest: a price will be reached. Werther thinks it should climb until it approaches the 50% premium Takeda paid to acquire Millennium. BH

problem was that Thousand Oaks, California-based Amgen was developing Vectibix (panitumumab) in head and neck cancer and first and second-line metastatic colorectal cancer. Given that Erbitux is a chimeric monoclonal antibody that inhibits epidermal growth factor receptor (EGFR) and Vectibix is a humanized monoclonal aimed at the same target, the prevailing thought was Amgen's product "seemed safer," says Carol Werther, analyst with Summer Street Research Partners.

That turned out not to be the case. In March 2007, Amgen discontinued the trial evaluating Vectibix in combination with standard chemotherapy and Amgen's Avastin (bevacizumab) in first-line mCRC, due to a statistically significant difference in progression-free survival in the control arm. Those data made it appear that "Vectibix was an inferior product," Werther says. "People started to think, perhaps these [EGFR inhibitors] aren't the same."

Then came news from ImClone partner Merck, of Darmstadt, Germany. The announcement in May of the phase 3 FLEX trial (with full data released at the American Society of Clinical Oncology meeting in June) showed that adding Erbitux to a platinum-based chemotherapy increased median overall survival by 1.2 months over chemotherapy alone in first-line treatment of non-small cell lung cancer (NSCLC). Werther says that although Avastin is approved

for NSCLC, "about half [of patients] can't take it," so the opportunity for a new product is there, and that indication alone could add another \$1 billion to Erbitux sales.

Factoring in the promise around Erbitux and considering ImClone's pipeline of five biologics aimed at oncology, buying ImClone "does make sense now," says Werther. (Though the price remains unclear, Box 1.)

As with the other recent biotech purchases (Table 1), a final factor is that ImClone and Genentech develop biologics, which have no generic competition yet on the horizon—a problem currently plaguing pharma's stable of small molecules. That helps explain the odd shift creeping across the drug development landscape. Katherine Kim, analyst with Banc of America securities in New York, points out that today's large-cap biotechs are performing the way pharma companies used to perform 5 or 10 years ago—recording growth quarter upon quarter. Underneath, the mid-caps now grow the way the large-cap biotechs did 5 or 10 years ago, making them targets for takeover, too.

Right now, "pharma is more motivated to buy to get that growth," Kim says. "If you need to have earnings growth, you need to go after companies that have marketed products. You can take clinical risks with your own pipeline."

Brady Huggett New York