# IN brief

## ATM cash for biotechs

In August, Somaxon Pharmaceuticals chose an alternative strategy to raise $30 million, and in June, BioCryst Pharmaceuticals of Research Triangle Park, North Carolina, used a similar tactic to raise $70 million. Both companies raised money through at-the-market (ATM) offerings, a financing tool that was not used at all in the biotech industry as recently as 2005. Since then, ATMs have been rapidly gaining favor. According to the New York-based investment bank Brinson Patrick Securities, which specializes in ATMs, by 2010 the number of ATM offerings had grown to 26 in the biotech sector (raising $184 million), nearly tripling the 9 that took place in 2009. This year there have been 15 so far. Biotechs typically raise capital by selling shares all at once in large tranches and at a fixed price, while relying on value-adding milestones, hoping that the cash can get them through to the next milestone. Instead, with an ATM offering, a company raises capital by selling shares in the open market at the prevailing price over a period of time, with the advantage that the sale of shares can be stopped or initiated at any time. Todd Wyche, founder and managing director of Brinson Patrick, thinks biotechs are shifting their approaches, using multiple financing options. "Instead of an episodic financing, relying on one or two traditional tools, we're seeing them incorporate a more strategic kind of financing strategy," said Wyche. Not only are ATM offerings more flexible, providing cash when needed, but they are also cheaper than traditional stock offerings in which warrants, underwriter spreads and discounts to the market price are taken into account. ATMs aren't the perfect solution, however. One drawback is that shares have to be dribbled into the market so large amounts of capital can't be raised quickly. But Brinson Patrick has found that issuers can sell 10–15% of the daily volume without adversely affecting the share price. The shares from an ATM offering also end up in the open market where investors may not be interested in holding them long term. Other options, such as standby equity distribution agreements offered by Yorkville Advisors of Jersey City, New Jersey, can provide the same flexibility while getting the shares into the hands of long-term investors (*Nat. Biotechnol.* **28**, 301–302, 2010). Michael J. Nowak, managing director of Yorkville Advisors, explains that as long term–only investors, they are always interested in maintaining a strong share price for the company. "In an ATM, [bankers] do not care, since they pick up their couple of percent commission on the trade regardless of impact or price," he adds. *Brian Orelli*

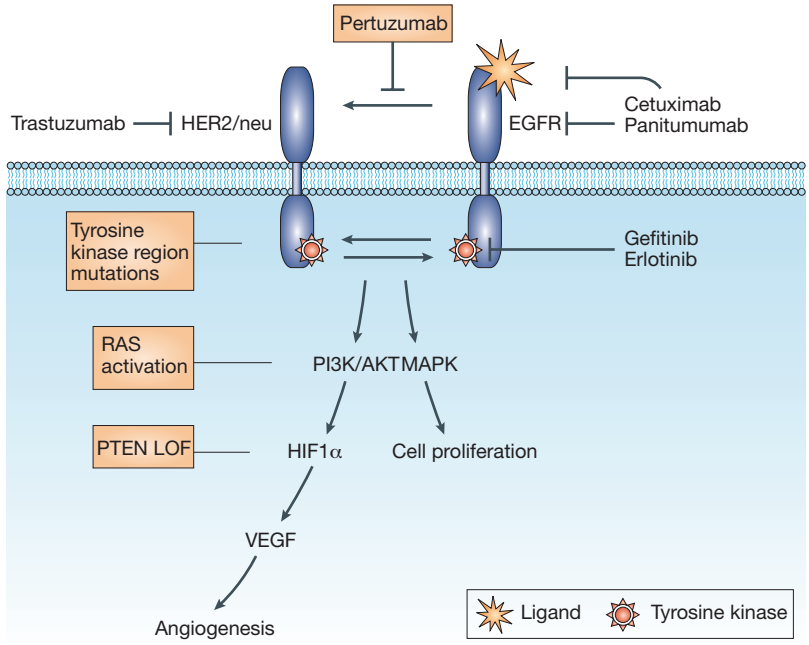


# Pertuzumab to bolster Roche/Genentech's breast cancer franchise?

In July, Genentech announced that its humanized monoclonal antibody (mAb) drug pertuzumab met its primary endpoint in a phase 3 trial of metastatic breast cancer patients also receiving the standard regimen of Herceptin (trastuzumab) plus Taxotere (docetaxel). The company, a subsidiary of Basel-based Roche, has so far revealed few details on the outcome of the combination trial, dubbed Cleopatra. Its terse disclosure simply stated the combination "significantly" extended progression-free survival in women with HER2-overexpressing metastatic breast cancer. The safety profile was consistent with previous studies of the two drugs, either as monotherapy or in combination. But anticipation over the drug's efficacy is mounting because, if successful, the new combination could extend the benefits of targeted therapy to HER2-positive patients, who either do not respond to or relapse on existing Herceptin-based regimens.

Genentech, of S. South Francisco, California, plans to unveil the details of the 808-women trial at this year's San Antonio Breast Cancer Symposium, in San Antonio, Texas, which kicks off on December 6. The company also plans to file for approval of the combination shortly after the presentation. It is difficult to judge at this stage whether Genentech will obtain approval solely on the basis of the Cleopatra study, which had progression-free survival as its primary end point. Recently, Genentech and the US Food and Drug Administration (FDA) have locked horns over this issue in connection with the approval of Avastin (bevacizumab) in breast cancer (*Nat. Biotechnol.* **29**, 669, 2011). "I don't think it should be impossible, but the data will have to be really, really good," says Elmar Kraus, analyst at DZ Bank in Frankfurt.

HER2 expression, which is associated with a poor prognosis, occurs in around 20% of invasive breast cancers (as well as in lung, ovarian, pancreatic and gastric cancers). In normal cells, the transmembrane tyrosine kinase is involved in cell survival and differentiation. Signaling events implicate four closely related HER family members. HER2 is recruited to a ligand-receptor complex comprising one of over ten neuregulin ligands and either HER1, HER3 or HER4. When aberrant expression of HER2, arising from gene amplification events, gives rise to high concentrations of HER2, this equilibrium is disrupted, leading to the protein becoming constitutively active. Thus, dimerization with other HER receptors—and subsequent signaling—can occur, even in the absence of ligand binding. "We think the oncogenic unit here is the higher order complex between HER2 and HER3," says Genentech senior staff




Pertuzumab exerts its therapeutic effects by inhibiting HER2 dimerization. The monoclonal antibody binds a different epitope on the HER2 receptor to Herceptin and blocks its activation. Adapted from *Nature Reviews Drug Discovery* **5**, 507-521 (June 2006).