safety," says Cowen analyst Sanderson. "I think there's a lot of excitement about the potential of the mechanism, but people are working with no clinical data at the moment."

Though New York–based Pfizer will have a stronger hand in Alzheimer's once it completes its acquisition of Wyeth, it already has one of the most intriguing late-stage Alzheimer's drug candidates in the form of Dimebon (latrepirdine), a compound with a 25-year history as an anti-histamine in Russia, which has demonstrated cognitive benefit in a phase 2 study (*The Lancet* 372, 207–215, 2008). Gandy and colleagues reported at last month's International Conference on Alzheimer's Disease in Vienna that Dimebon, surprisingly, increased the release of beta amyloid from cultured nerve cells and isolated nerve terminals, and it raised levels of beta amyloid in the brains of transgenic mice expressing human amyloid precursor protein. The compound interacts with multiple receptors, including several serotonin (5-hydroxytryptamine) receptor subtypes. Gandy admits that the work raises more questions than it answers. "I think that if the cognitive benefit is confirmed [in the phase 3 trial], then dissecting the molecular basis for the mechanism of action will take on major importance," he says.

Although the amyloid hypothesis can claim quite an amount of scientific validation, it still harbors several mysteries. "My guess is that anti-amyloid therapies would be much more successful as prophylaxis, but getting from here to there is a challenge. I'm still a believer, but the absence of any signal from any of the trials to date is discouraging," Gandy says.

Cormac Sheridan *Dublin*

Box 1 Saving Elan

The Johnson & Johnson (J&J; New Brunswick, New Jersey, USA) deal is a life preserver for Elan, which has been in financial trouble since last summer, when it revealed that the phase 2 trial of bapineuzumab (AAB-001) had missed it primary endpoints, albeit with some efficacy in certain patient subgroups. Days later, Elan also announced that two more patients taking its multiple sclerosis drug Tysabri (natalizumab) had contracted the potentially fatal brain disease progressive multifocal leukoencephalopathy. These events combined to drive down Elan's stock from more than $33 last summer to less than $10, where it still languishes today.

Elan ended 2008 with about $375 million in cash and equivalents. With the summer's bad news still hanging around its neck (and stock price) and expecting to spend around $350 million in R&D this year, the company needed to hunker down. In January, it hired Citigroup to review "strategic alternatives," including a merger or an outright sale of the company. In the first quarter, it closed offices in New York and Tokyo. In February, it also cut 230 positions (~14% of the total workforce), including research and clinical development positions, and looked to further curtail spending by saying it would "reassess" investing in a biologics manufacturing facility and suspending fill-finish activities in preparation for launching bapineuzumab until after the phase 3 results are known.

Despite these savings, Elan has still been wrestling with how to pay for its promising—though expensive—lead product in Alzheimer's. Last year, Elan spent $113 million on its Alzheimer's Immunotherapy Program (AIP), partnered with Wyeth (in the process of being purchased by Pfizer), and estimated it would spend as much as $500 million on bapineuzumab and the rest of the portfolio over the next three or four years. This was looking more and more impossible for Elan, given its dwindling cash position and a troubling net debt of $1.4 billion.

The J&J deal solves both problems. First, J&J takes over the AIP, which includes the intravenous formulation of bapineuzumab, as well as a subcutaneous version and an Alzheimer's vaccine (AAB-001), in phase 2 development. J&J will build a new joint venture around AIP and own 51.1% of it (with Elan holding the rest), and J&J will dump up to $500 million into development, thus relieving Elan of about $100 million in annual R&D expenditure. Second, J&J invested $1 billion into Elan itself, receiving about 18.4% of Elan's outstanding shares in return—making it the largest shareholder. This influx of cash will allow Elan to reduce its net debt by 70%, to $400 million. Elan believes that the reduction in R&D spending, coupled with an expected growth in Tysabri sales, will allow the firm to post a pre-tax profit and be cash-flow positive by the end of 2010.

Brady Huggett

IN brief

Virus stalls Genzyme plant

Genzyme of Cambridge, Massachusetts, faces millions in lost revenue from its top-selling specialty drugs Cerezyme and Fabrazyme as result of a viral contamination at its Allston, Massachusetts plant. The company has announced that it will temporarily shut down the facility owing to a bioreactor contamination with Vesivirus 2117, which does not cause human infections, but impairs growth of the biologics-producing Chinese hamster ovary (CHO) cells. It reportedly originated from tainted nutrient medium and belongs to the same strain that caused delays at the Allston site and its European biologics plant in Belgium last year. Genzyme anticipates supply constraints of Cerezyme (imiglucerase), a treatment for Gaucher disease, and Fabrazyme (agalsidase beta), used to treat Fabry disease, while the facility shuts down for 6 to 8 weeks to allow decontamination. Although Genzyme also produces Myozyme (alglucosidase alpha) at the plant, no runs were scheduled during the presumed period of shutdown so supplies of that drug will not be affected. With sales of $1.2 billion for Cerezyme and $494 million for Fabryzyme in 2008, analysts estimate the manufacturing crisis will result in $100–300 million in lost sales. The US Food and Drug Administration (FDA) has contacted rival manufacturers Shire of Basingstoke, UK, and Carmiel, Israel–based Protalix, who have enzyme replacement therapies for Gaucher disease in clinical trials, to file treatment protocols, which would allow physicians to use their drugs ahead of approval. The situation could also boost sales of Allschwil-based Actelion's Zavesca (miglustat). *Victor Bethencourt*

Stem cell funding widens

The National Institutes of Health (NIH) issued new guidelines for federal funding eligibility of human embryonic stem cell (hESC) research, loosening almost a decade of constrained financial support for academic researchers. Under the new rules, which took effect July 7, the NIH will establish a registry of fundable lines to which scientists can apply for inclusion. Stem cell lines derived before this date will be reviewed case by case for eligibility. In March, President Barack Obama lifted restrictions on hESC research established by the Bush administration (*Nat. Biotechnol.* **27**, 407, 2009), and requested the NIH draw up new rules. The draft guidelines released in April, established that fundable research must be limited to in vitro fertilization leftovers, and this requirement remains unchanged in the final guidelines. But outdated informed consent rules included in the draft, which would have forced laboratories to discard valuable lines, have been revised. Some restrictions remain, such as the exclusion of stem cells derived from embryos created for research, though overall, researchers are satisfied. "The new guidelines will hopefully open new opportunities for grants on the new lines, reduce some of the administrative burdens in the lab, and be better all around for our science," says George Daley, director of stem cell transplantation at Children's Hospital in Boston. *James Netterwald*