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PAOLO VESCIA

New Alzheimer's theory may shift funding targets

Anti-plaque push may lose favor

BY RON LEUTY
San Francisco Business Times

New Alzheimer's disease research from Genentech Inc. and the Buck Institute for Age Research is challenging a decade-old theory about how the brain disease begins and, as a result, helping shift Alzheimer's funding.

Alzheimer's drug-development programs and treatments have largely focused on eliminating sheaths of plaque that form on the brains of the roughly 27 million people worldwide who have the disease. That focus has created a sort of "Alzheimer's mafia," as some call it, that has kept research dollars flowing toward plaque treatments — sometimes at the expense of alternative theories.

But some high-profile failures by plaque-fighting drugs over the past two years may cause scientists and funders to look anew at findings like those from South San Francisco-based Genentech and Novato's Buck Institute. Regardless, researchers say there are new ways of looking at how Alzheimer's starts and progresses in addition to studying plaque.

"There's lots of work to do," said Marc Tessier-Lavigne, executive vice president of research drug discovery at Genentech. "(But) this smells right."

Tessier-Lavigne and Genentech researcher Anatoly Nikolaev found that a protein long implicated in the formation of plaque clips unneeded nerve endings in the early formation of the brain.

Alzheimer's researchers had never explained why amyloid-producing protein, or APP, is in the brain in the first place.

Meanwhile, the Buck Institute in Novato and its French partners believe that Alzheimer's is caused by an imbalance of the protein and netrin-1, another protein that guides nerves in making or breaking memory connections in the brain.

The factors that throw the proteins out of balance could be similar to those for heart attack risk: diet, exercise, genetics or a head injury, said Dale Bredeesen, who led the Buck Institute's research collaboration with a French team.

"We're not saying amyloid is wrong. There's just a much bigger picture here," Bredeesen said. "Amyloid is the tip of the iceberg. Now we say here's some more of the iceberg."

Indeed, Genentech is playing both sides of Alzheimer's — partner AC Immune SA of Switzerland has an anti-plaque drug in a Phase I trial.

But some potential anti-plaque treatments have not shown great results. The drug bapineuzumab, developed by Wyeth and South San Francisco's Elan Corp., has been linked to brain swelling in a few patients in a mid-stage trial.

There is no medication to halt Alzheimer's, and current treatments only slow memory loss for a year or less.

"It may be necessary to tackle more than one cause," Tessier-Lavigne said. "We don't understand enough about the disease."

Yet the multi-pronged approach, many say, has been largely pushed aside by funding organizations like the National Institutes for Health, foundations and Big Pharma because plaque is so obviously present in the Alzheimer's patients' brains.

"That's where there's the most money," said Elliott Mufson, a professor of neurological sciences at Rush University Medical Center.

Yet, a few companies, like Medivation Inc. of San Francisco, are making breakthroughs on scientific and financial fronts. The company's Phase III Alzheimer's and Huntington's Disease treatment, Dimebon, could inhibit brain cell death as well as stimulate the growth of nerves from brain cells.

Dimebon's results to date attracted Pfizer Inc., which paid \$225 million upfront and could pay up to \$500 million in development and commercial milestones for Dimebon.

Merck & Co. also is backing research at the J. David Gladstone Institutes in San Francisco that is looking at drugs that could stop a particular apoprotein, called apoE4.

"There's been a growing sense that it's risky in a big disease like Alzheimer's to put all your eggs in one basket," said Murali Doraiswamy, a memory expert at Duke University and a medical adviser to the Alzheimer's Foundation of America. "We need multiple targets in this disease."

rleuty@bizjournals.com / (415) 288-4939 ■

Banks worry over stricter revised TARP regulations

BY MARK CALVEY
San Francisco Business Times

The Obama administration is stepping up its oversight of the government program to invest in the nation's banks.

The Treasury Department's most recent bank recovery plan included a clause that exempted banks who previously took government money under the Troubled Asset Relief Program from restrictions later adopted. That exemption appears to have been nullified in the federal stimulus package signed into law Feb. 17.

Increased restrictions placed on TARP recipients that may now apply to all those who have already accepted money include limiting quarterly dividends to a penny per share; making cash acquisitions of other 'healthy' banks; buying back shares; participating in federal foreclosure prevention efforts; and limiting executive compensation to no more than \$500,000.

Not surprisingly, many bankers — and their attorneys — are waiting for the Treasury to provide more details on how the TARP program will be affected by the retroactive changes adopted in the stimulus package.

"In general, community bankers are reading through the stimulus legislation and trying to figure out what it all means. It's a pretty big package," said Steve Brown, president and CEO of San Francisco-based Pacific Coast Bankers' Bank, which provides services to more than 500 community banks nationwide.

Several Bay Area community banks have received TARP money including Bank of Marin, Bridge Bank and Community Bank of the Bay.

Another, Boston Private Financial Holdings, parent of San Mateo-based Borel Private Bank & Trust, was among the first wave of banks to receive TARP money. Boston Private received \$154 million in TARP funds in late November.

"We down-streamed these funds to

our banking affiliates, which is allowing them to further expand their lending programs," said spokeswoman Catharine Sheehan. Total loans increased 2 percent during the fourth quarter of 2008 to \$5.5 billion and were up 4 percent on a year-over-year basis.

That increased lending may explain why several community bankers were eager to get their hands on TARP money even though much of the public's attention on TARP has focused on regulators grappling with the deepening woes facing Citigroup, Bank of America and other major players.

In a Feb. 6 letter sent to banks, TARP's Special Inspector General Neil Barofsky said he wanted a response within 30



Conover

days outlining how each TARP recipient is using the money, whether the money was kept separate from other capital and how the bank actually used — or plans to use — the money.

"We think this initiative is vital to providing the transparency (for) the TARP program," Barofsky said in his letter.

John Conover, president and CEO of Borel Private Bank & Trust, said his bank is focused on using the TARP money received by the bank's parent, Boston Private, to make more loans.

"We're still lending money," Conover said. "We're traditional bankers, taking deposits, making loans and requiring down payments."

That can be a successful formula. In one of the worst years for American banking, Borel prospered in 2008. "For Borel Private Bank & Trust Co. it was a year to be remembered and repeated," Conover said. "Borel experienced its best financial results ever recorded in our 28-year history."

mcalvey@bizjournals.com / (415) 288-4950 ■

Southern Wine to build warehouse

BY BLANCA TORRES
San Francisco Business Times

Southern Wine and Spirits won approval from Union City to demolish an existing facility and build a 75-foot-high, 400,000-square-foot warehouse.

The beverage company plans to raze its 188,000-square-foot facility at 1555 Atlantic St. to make room for the new construction. It also owns a 300,000-square-foot office and warehouse building and leases 288,000 square feet on Dowe Avenue. The Miami-based firm is one of the nation's largest beverage distributors with its Northern California headquarters in Union City. Southern Wine declined to comment.

The new state-of-the-art facility will allow Southern Wine to bring all of its warehouse operations under one roof to save space and money. It will continue to use the building on Dowe Avenue that it owns for office and storage.

Southern Wine moved to Union City twenty years ago and is now the city's largest employer, with about 1,150 workers. Carmela Campbell, a Union City plan-

ner, said the company says it does not plan to lay off workers after the consolidation and expects business to increase.

The idea of building higher-density industrial fit with a provision added recently to the city's general plan.

"As cities become more and more developed, this is what companies are going to have to do to stay in the Bay Area," she said. "The goal is to keep business in the Bay Area. It's best for everybody, the environment, the community and jobs."

Union City has close to 14 million square feet of industrial space, which is about 9 percent of the Interstate 880 industrial corridor, according to Cornish & Carey. Joe Fabian, a broker with Cornish & Carey's Hayward office, said most large users that want to build new sites end up going to the Central Valley, for more space and less expensive land.

"The fact that Union City supported it is smart," Fabian said. "When you're as big as Southern Wine and Spirits, there are not that many alternatives."

btorres@bizjournals.com / (415) 288-4960 ■