

Living Up to its Acronym, ACT Nears Telatinib Phase III

By Tom Wall
Staff Writer

The "ACT" in ACT Biotech Inc. stands for "accelerate cancer therapeutics" and the 3-year-old San Francisco-based company is living up to its acronym as it nears the start of a Phase III trial in the second half of this year of lead candidate telatinib in combination with chemotherapy for the first-line treatment of advanced stomach cancer.

Privately held ACT was founded in early 2008 by Ali Fattaey, president and chief operating and scientific officer, and Wolf Busse, who recently retired as CEO.

Fattaey had two decades of cancer research, drug discovery and development experience, including helping start the Melanoma Therapeutics Foundation in San Francisco, work with RAF kinase inhibitors at Onyx Pharmaceuticals Inc., of South San Francisco, and duty as chief scientific officer at Sagres Discovery, of Davis, Calif.

Busse spent 28 years at Bayer Pharmaceuticals, including time as general manager of the Bayer Healthcare biotechnology unit, in Berkeley, Calif., before leaving in 2004 to start Bayer spinoff Aerovance Inc., also of Berkeley, and later to run the Melanoma Therapeutics Foundation and serve as a venture partner at NGN Capital.

The Bayer and NGN connections were key. Telatinib and three other oncology candidates upon which ACT was founded were originally developed by Bayer Pharmaceuticals. ACT licensed them in 2008 following Bayer's merger with Schering AG and the decision to close Bayer's U.S. R&D operations.

Bayer had done the preclinical and early clinical development of telatinib, including what Fattaey described as an expensive Phase I trial, and manufacturing was advanced.

"Telatinib came as a fairly mature package and program," Fattaey said. ACT operates independently of Bayer, but Bayer holds a minority stake in ACT as part of the licensing agreement, he said.

Venture investor NGN Capital backed the start-up with a \$12 million Series A tranched through 2008 and an additional \$3 million in 2010. ACT secured an additional \$3.5 million through a venture debt financing vehicle. Today the company has seven employees, all in San Francisco, and

using a virtual operating model, about twice as many consultants.

Fattaey said that he expects that model and the size of the organization could change as ACT gets into Phase III with telatinib, a highly selective orally available antiangiogenic therapeutic that targets the VEGFR and PDGFR receptor tyrosine kinases to inhibit the blood supply to tumors.

He noted that telatinib has demonstrated in earlier studies that it is safe and tolerable at full dose in combination with chemotherapy – something the company thinks sets it apart. "That's what really attracted us to the drug," Fattaey said.

In January ACT reported at the American Society of Clinical Oncology (ASCO) Gastrointestinal Cancer Symposium, in San Francisco, new data from its Phase II trial of telatinib that the company said supported the ability to continuously dose telatinib in patients with stomach cancer combined with full-dose, standard-of-care chemotherapy.

In addition, morphological data from radiographic scans of tumor response demonstrated a unique and characteristic feature of potent antiangiogenic activity from treatment with telatinib, verifying the on-target effect of the drug, the company explained.

That followed an October presentation of Phase II data at the European Society for Medical Oncology meeting in Milan, Italy, showing that telatinib achieved a 66 percent overall response rate in gastric cancer and that it was well tolerated and demonstrated evidence of antiangiogenic activity.

Telatinib also was studied in two Phase I monotherapy and four Phase Ib combination therapy trials in more than 250 patients. Results demonstrated that telatinib could be combined with taxane, platinum, fluoropyrimidine and topoisomerase chemotherapies at full dose without pauses in treatment.

ACT in late February filed a special protocol assessment with the FDA for the telatinib stomach cancer trial. Fattaey said the company is still in discussions

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with the FDA, but exchanges have been very positive. The company also has received feedback on the Phase III trial design from the European Medicines Agency, he said.

The trial will be a multicenter, double-blind, randomized trial comparing telatinib in combination with a standard regimen of chemotherapy vs. chemotherapy alone in advanced stomach cancer patients.

Most investigators will be in Europe and the Americas, Fattaey said. He expects the trial to take about 30 months, which could mean a possible new drug application filing by the end of 2013 or into 2014.

Telatinib, which has received orphan drug designation from the FDA for gastric cancer, also has been studied in solid tumors including colorectal and kidney cancers, but Fattaey said there is an extreme unmet need in stomach cancer, which with 865,000 annual deaths globally, is the second leading cause of cancer death. Stomach cancer typically is detected late, and most patients do not respond to standard chemotherapy.

Fattaey said that ACT is in discussions with potential late-stage development and commercialization partners for telatinib, but he expects ACT to have a continuing role in funding and advancing the program.

Besides telatinib, ACT's pipeline has three other oncology candidates.

Fattaey said ACTBI003, an oral kinase inhibitor with multiple modes of action, is ready for Phase I trials this year, and has potential for treatment of multiple cancer indications.

ACTBI010, a selective oral inhibitor of mitotic kinases Aurora A and Aurora B, has shown excellent safety in preclinical experiments and achieved tumor regressions in solid and hematological tumor models.

Preclinical candidate ACTBI011 is an oral inhibitor of mutant BCR/ABL tyrosine kinase, including T315I mutant, which the company said will initially be targeted for leukemia patients who are resistant to imatinib, dasatinib and or nilotinib. ■