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Financings Roundup

Tygacil by the Tail? Tetraphase IPO: $86M for New Antibiotics

By Randy Osborne
Staff Writer

Looking to bolster its planned Phase III trial with TP-434 (eravacycline) for complicated intra-abdominal infections, Tetraphase Pharmaceuticals Inc. filed for an initial public offering (IPO) that would raise up to $86.2 million, though neither the targeted number of shares nor the price of each was disclosed.

In February 2012, the company landed a $67 million federal contract for the broad-spectrum antibiotic from the Biomedical Advanced Research and Development Authority, which came six months after a $36 million National Institutes of Health (NIH) contract for a separate, respiratory antibiotic, TP-271.

Only one new compound in the tetracycline class, Tygacil (tigecycline, Pfizer), has been approved in more than 30 years, mainly because semi-synthetic production methods hinder chemical diversity. Tetraphase's approach wants to change that.

TP-434 is a fully synthetic tetracycline antibiotic, created using Watertown, Mass.-based Tetraphase's tetracycline chemistry platform, licensed from Harvard University. Positive Phase II data were unveiled in September 2012.

Intended for Gram-negative and Gram-positive pathogens, TP-434 targets bugs such as *Escherichia coli* and *Klebsiella pneumonia*, in the former category, as well

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BIO CEO & Investor Conference

Partnering Your Way to M&A? Keep Cash Balance, Options

By Jennifer Boggs
Managing Editor

NEW YORK – How does a biotech company look to set itself up as a potential acquisition target down the road? The answer, according to a panel at this year's BIO CEO & Investor Conference, is that it depends.

On financing, on the indications, the market size and the internal pipeline of prospective acquirers, just to name a few variables. There are, however, a couple of certainties. One, the number of M&A deals has dropped in the past

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StemCells: Spinal Injury Gains Are Sustained After One Year

By Catherine Shaffer
Staff Writer

StemCells Inc. reported positive results from the first patient cohort of a Phase I/II trial of its human neural stem cell product for spinal cord injury, and investors responded enthusiastically, driving the Newark, Calif.-based company's stock up 21 percent.

Out of three patients with complete, chest-level spinal injury, two had regained sensitivity to heat, touch and

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NewCo News

Swiss Start-up Piqur Developing Dual PI3K-mTOR Inhibitors

By Cormac Sheridan
Staff Writer

Matthias Wymann, the Swiss scientist who discovered the first phosphoinositide 3-kinase (PI3K) inhibitor, is co-founder of a new cancer drug discovery start-up, Piqur

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Lycera Expands Partnership With Merck for Potential $600M

By Catherine Shaffer
Staff Writer

Lycera Corp. doubled its sweet 2011 deal with Merck and Co. Inc., of Whitehouse Station, N.J., in a new agreement designed to expand on the companies' prior relationship, which has centered on retinoic acid-related orphan receptor (ROR[gamma]t). Lycera will receive an undisclosed up-front payment and research funding,

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Piqur

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Therapeutics AG, which recently completed a seed financing round that will enable it take forward a pipeline of next-generation kinase inhibitors.

The company, a spinout from the University of Basel, where Wymann is based, is developing dual inhibitors of PI3K and mammalian target of rapamycin (mTOR). It has assembled a veritable who's who of scientific staff and advisers, who have played leading roles in the development of the field.

The other co-founders include company chairman Bernd Giese, a high-profile organic chemist best known for his work on electron charge transfer in DNA and peptides; CEO Vladimir Cmiljanovic, who spent his scientific research career with Giese and Wymann; and Andreas Emmenegger, chief financial officer of Molecular Partners AG, of Zurich, Switzerland. Its chief scientific officer is Doriano Fabbro, formerly head of kinase biology at Novartis AG, of Basel, Switzerland. Its scientific advisory board includes Michael Hall, of the University of Basel, who discovered TOR.

About 20 years ago, Wymann identified PI3K as the target of wortmannin, a fungal metabolite known for inhibiting respiratory burst (or oxidative burst) activity in neutrophils. (Seattle-based Oncothyreon Inc. is conducting Phase II trials in multiple cancer indications of a semi-synthetic derivative, PX-866l.)

Over the past decade, Wymann and his team have assisted several large pharma firms in the discovery and development of PI3K-Akt-mTOR pathway inhibitors. The pathway plays an important role in down-regulating apoptosis and prolonging cell survival. Aberrant signaling or amplification of the pathway is a significant feature of many cancers.

BEZ235 was the first dual inhibitor of PI3K and mTOR to reach the clinic. Novartis is now conducting Phase II trials of the compound in multiple cancer indications. Paris-based Sanofi SA is also in the clinic with a dual inhibitor, SAR245409 (XL765), which it in-licensed from Exelexis Inc., of South San Francisco.

Piqur has identified a series of compounds with attractive profiles using high-throughput screening, combined with in silico modeling and X-ray crystallographic analysis.

"What Piqur has today are molecules, which have significantly improved physico-chemical properties, leading to the improved pharmacological properties," Cmiljanovic told *BioWorld Today*.

The compounds exhibit strong PI3K inhibition and weaker mTor inhibition, in contrast to BEZ235, a compound which some of the Piqur team worked on during its preclinical characterization. "BEZ235 is a stronger mTor inhibitor than it is a PI3 kinase inhibitor," Cmiljanovic said.

However, excessive mTOR inhibition leads to the loss of negative feedback loop, which, ultimately, leads to an unwanted activation of PI3K signaling. Yet some level of mTOR inhibition has a synergistic effect on shutting down signal through the pathway.

Piqur has identified what it believes will be finely tuned dual inhibitors that do not reactivate the PI3K signal.

"We call it balanced inhibition. We think efficacy can be improved if you have a balanced way of inhibiting the two enzymes," Cmiljanovic said.

The company has also opted to focus on dual inhibitors with pan-PI3K selectivity in order to maximize their potential range of indications.

Drugs that target only one of the four Class I PI3K isoforms that are important in cancer, such as GS-1101 (CA-101), the Phase III PI3K delta inhibitor Foster City, Calif.-based Gilead Sciences Inc. acquired in its takeover of Calistoga Pharmaceuticals, have more limited application. "All isoforms are involving in cancer signaling pathways," Cmiljanovic said.

Although Piqur's kinase inhibitors can act on all four PI3Ks, as well as the two kinase activities present in the two mTOR complexes, they do not appear to affect the hundreds of other kinases that are involved in myriad signaling roles. "We know that our front-runner compound doesn't have specific off-target activities according to the preclinical compound characterization," Cmiljanovic said.

Piqur – the name is a play on PI3K, the concept that one in three people have a lifetime risk of developing cancer and the notion of a cure for cancer – has not disclosed the size of its initial funding round. Its investors are high-net worth individuals with significant experience in the life sciences industry. The funding will enable the company to advance its operational set-up, complete preclinical development of its lead compound, PQR-309, and prepare for its first clinical trial, which could commence later this year. ■

Other News To Note

• **MiReven,** of Perth, Western Australia, reported the publication of an in vitro study where the microRNA miR-7-5p significantly inhibited the migration and invasion of metastatic melanoma cells in the journal *Biochemical and Biophysical Research Communications*. In the study, miR-7-5p expression was shown to be reduced in metastatic melanoma-derived cell lines compared with primary melanoma cells. When the microRNA was reintroduced and expressed ectopically, migration and invasion of the melanoma cells was significantly inhibited in vitro. The study authors also investigated the mechanism of miR-7-5p and found that insulin receptor substrate-2 (IRS-2) is a functional target of miR-7-5p, which then decreases activity in the protein kinase B (Akt) signaling pathway, a key regulator of many oncogenic processes including cell migration.

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