PIQUR Therapeutics AG

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PIQUR
TARGETED CANCER THERAPIES

PI3K pioneers and pharmaceutical veterans take on mTOR's challenges

PIQUR Therapeutics' PI3K-Akt-mTOR–focused development strategy is strengthened by a team of kinase pioneers and blockbuster oncology program veterans; a powerful, targeted lead drug; and a strong intellectual portfolio.

Looking through the résumés of the cofounders and management of PIQUR is like reading a history of oncology drug development. Work performed by cofounders Bernd Giese and Matthias Wymann gave a new impetus to kinase drug research, combining chemistry and biology at their best, while members of the C-suite played pivotal roles in the development of cancer drugs such as Afinitor, Glivec/Gleevec, Tasigna, Femara and MabThera. The organization is steeped in the history of oncology drug development and the pharmaceutical culture of Basel, Switzerland.

This team of veterans from oncology programs at the likes of Novartis and Roche has come together to work on one goal: creating targeted cancer therapies for orphan indications and other areas of unmet need. Led by Vladimir Cmiljanovic—who worked on PI3K programs sponsored by pharmaceutical companies, such as Novartis, while pursuing his PhD at the University of Basel—PIQUR has raised money from private investors and a highly respected healthcare venture capital firm, Versant Ventures. This has allowed the company to move its lead drug into phase 1 quickly while following the thorough, no-shortcuts model of research.

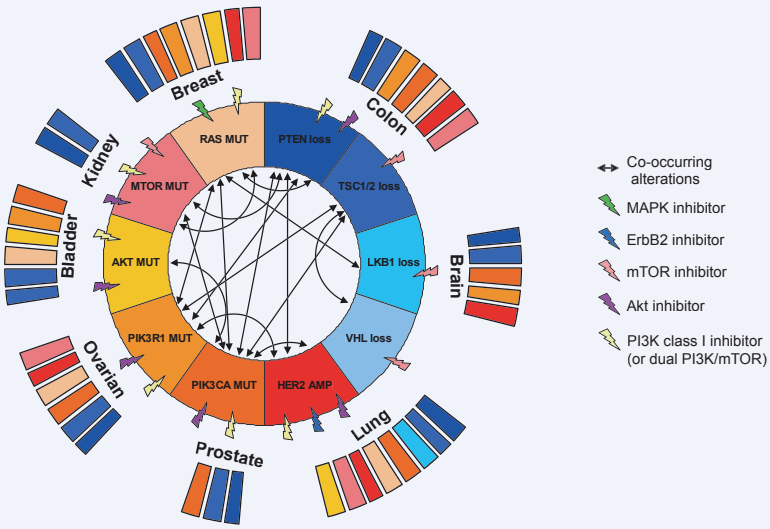

Figure 1: Dual inhibition. Dysregulation of the PI3K-Akt-mTOR pathway is observed in 80 per cent of tumors. Genetic alterations shared by different cancer types are shown in the outer circle. The ability of PQR309 to target both the PI3K and mTOR results in more stringent inhibition of the pathway in several tumors compared to other therapeutic agents.

A dual, balanced PI3K and mTOR inhibitor

Since its inception in 2011, PIQUR has been able to attract a team who knows how to develop a drug the Basel way and raise $42 million to fund the work because of the strength of its science. Cmiljanovic spun the program out of the University of Basel laboratory at which he worked with Giese and Wymann. The company focuses on PI3K-Akt-mTOR, a pathway linked to cell proliferation, survival and migration that has been medically validated by approved drugs from Gilead and Novartis.

Earlier generations of PI3K and mTOR inhibitors suffered from an array of shortcomings, such as low solubility or the tendency for patients to develop resistance. Scientists at PIQUR understand these flaws and have used them as guideposts when designing the company's lead drug, PQR309. The drug is an oral therapy that fully inhibits all four isoforms of PI3K with no off-target effects. mTOR is also inhibited but at a slightly lower level than PI3K to prevent unintended feedback.

PQR309's ability to fully inhibit all four isoforms of PI3K, plus mTOR, without causing off-target effects, is due to a very high level of selectivity which makes it an attractive choice for use as a monotherapy, or in combination with new or existing drug therapies (**Fig.1**). Unlike most of its competitors, PQR309 crosses the blood-brain barrier, expanding its use beyond solid tumors and lymphomas and into brain cancers. PQR309 also boasts enviable drug-like properties, such as excellent solubility, and has performed as expected in early clinical trials.

PIQUR is running a phase 1 trial of PQR309 in solid tumors at five sites located in Switzerland, Spain and the United Kingdom. Dose escalation has gone smoothly with no unexpected adverse events, just the predicted and controllable side effects associated with PI3K inhibitors. Clinical trials in lymphoma and brain cancer are also planned. PIQUR has a clear vision of its development pathway for each indication through proof of concept and beyond.

From development to market

A US-FDA investigational new drug (IND) application for the next stage of development is already in place. The trial for solid tumors is ongoing.

Beyond PQR309, PIQUR has a backup cancer candidate with slightly different characteristics than its lead drug and preclinical programs targeting inflammation, ophthalmology, dermatology and central nervous system indications. PIQUR has scientific evidence that PI3K-Akt-mTOR is involved in these indications and is looking for co-development partners for its non-oncology programs.

The intent within PIQUR is to see PQR309 is brought to market quickly and efficiently. The lead drug is fully funded through to proof-of-concept data. Before the readout PIQUR may pursue a series B round or other means to raise money for later-stage development. If a serious buyout or out-licensing deal was proposed and would help bring PQR309 to patients faster and in more indications than currently envisioned, PIQUR might consider the offer.

Such business decisions have no impact on the day-to-day work at PIQUR, which from the board of directors down is focused on realizing the full potential of the PI3K-Akt-mTOR pathway. The concentration of talent at PIQUR and its focus on the pathway—even its name is a play on 'PI3K', 'quality' and 'cure'—mean few, if any, organizations are as well placed to handle this task.

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