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Samumed CMO Hopes To Reach Drug Approvals Via The Wnt Pathway

By Sten Stovall

THE CLINICAL-STAGE BIOTECH HAS DIVERSE PIPELINE generated by its Wnt signalling pathway technology platform, and aims to get its first drug to market in 2020.

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Privately held Samumed LLC, which is developing novel small molecule Wnt inhibitors for a variety of indications, has eight drugs in its pipeline based on that signalling pathway and believes its first could come to market in 2020, an event that would likely prompt the San Diego-based biotech so seek a stock market listing, its chief medical officer told Scrip.

Being able to harness the Wnt pathway is believed to be a key process in regenerative medicine, which could lead to therapies that reverse the development of numerous degenerative diseases.

Can Samumed Win With Wnt?

Many unsuccessful attempts have been made to harness the signalling pathway for drug development. Samumed believes it can succeed in that quest where others have failed, after having demonstrated clinical and preclinical proof-of concept in multiple disease areas with multiple drug candidates.

"It's been known for 30 years that the Wnt pathways is the key driver for tissue replenishment and tissue health in mammals," Samumed's chief medical officer Yusuf Yazici said in an interview.

"People have tried to drug the wnt pathway before for various indications – especially in oncology – as around 40% of all cancers are caused by multiple mutations in the wnt pathway. For example, more than 90% of colorectal cancers are caused by mutations in the Wnt pathway. So, much of the research into the Wnt pathway has been done in oncology."

Samumed's first focus was discovering first-in-class oncology drugs targeting cancers driven by mutations in the Wnt signaling pathway.

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> **- Samumed Chief Medical Officer**

It developed a proprietary platform through a process of identifying previously unknown biological targets of the Wnt pathway, designing unique combinations of these targets for specific disease indications, and then developing small-molecule drugs to treat them with.

In Nov. 2017, Samumed announced data from a Phase II clinical study of lead drug candidate, SM04690, which showed the ability to regenerate cartilage in knee osteoarthritis; Phase IIb results are due mid-2018.

The company's research is showing that in addition to slowing the degenerative process in cells marked with disease, healthy cells are regenerating, replacing those that are damaged.

After discussions with the FDA, if the proof-of-concept study is positive across both doses, the company will initiate two Phase III studies in the second half of 2018 and seek approval around the end of 2019.

"We have now finished two Phase II trials for SM04690, the first showing proof-of-concept and the second - which has just completed - was for dose finding, Yazici explained.

"Our plan is that the readout from the latest Phase II trial will come in early June and we'll then go to the FDA in early autumn to discuss the two pivotal Phase III trials that will be needed, which will hopefully lead to approval; we plan to start those pivotal trials in early 2019. The two pivotal trials will be almost identical in design because the FDA want to reproduce stability of the response to the therapy," he said.

Drug Duo Race Looms

That scenario would put SM04690 on track to becoming Samumed's first marketed therapy in the second half of 2020 - provided its investigational oncology compound SM08502 doesn't pip it to the post through an accelerated regulatory pathway, the company's CMO said.

SM08502 is currently in Phase I trialing for solid tumors and pancreatic, ovarian and hepatocellular cancers.

"In the US there is the possibility for an accelerated pathway for SM08502. There the regulatory pathway for oncology candidates, especially hard-to-treat cancers like pancreatic cancer, involve end-of-Phase I meetings with the FDA; there the request could be made to progress SM08502 to pivotal Phase II trials and then get approval after that," Yazici told Scrip.

"So our SM08502 might be sped up if the Phase I trial shows similar efficacy as that seen in trials in animals. That could mean our candidate in oncology overtakes SM04690 in osteoarthritis. But for the moment it looks most likely that we'd get approval in osteoarthritis first, in late 2020. But oncology shouldn't be far behind," he said.

Samumed has five different small-molecule drugs in seven different disease indications (when counting all oncology indications as one) that are currently being tested in humans. All of its compounds and intellectual property are internally-developed and exclusively owned. Its pipeline has shown promising therapeutic activity and good safety profiles in treating osteoarthritis, cancer, degenerative disc disease, psoriasis, Alzheimer's disease, idiopathic pulmonary fibrosis, tendinopathy, and as an anti-wrinkle therapy.

The company, which expects multiple FDA approvals over the next few years, has so far raised more than $300m of private capital.

Partnering some of its assets with bigger pharma players is a likely option, it says.

"Yes, we are open to potential partnering, and have already been speaking to some companies," Yazici said, without elaboration.

'No One-Trick Pony'

Founded in 2008 as a joint venture with Pfizer Inc., Samumed may decide to make an IPO once its first compound gets the green light from US regulators.

Its CMO says the Wnt specialist would then be an attractive proposition for investors.

"We're no one-trick pony; We actually have a treatment platform that has generated drugs for different diseases in different types of organs which do not just address the sign and symptoms of conditions, but which have mechanisms of action that treat the underlying disease, hence it's termed 'disease modifying' therapies," Yazici said.

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