at a glance™

Of Note: Interim data from a Phase 2 lung cancer study of Vaccinex's lead candidate, VX15, in combination with Merck KGaA's Bavencio® produced progression free survival (PFS) in 63 percent of 16 patients who failed prior checkpoint therapy. A second cancer collaboration with two more checkpoint inhibitors is underway with Bristol-Myers Squibb with data releases expected to begin 1Q20. A potentially pivotal Phase 2 registration trial in Huntington's disease is underway with top-line data due next year.

Key Considerations

- **In an interim analysis of the Phase 2 study of combination VX15-Bavencio (reported at ASCO, June 1, 2019), 63 percent of patients (10/16) whose tumors had progressed during or following treatment with a checkpoint inhibitor (mostly Keytruda) benefited after switching to study drug, an early but very encouraging finding.**
- **Fifty percent of the responders (5/10) have been on study drug for four months or longer. Additional interim data is expected 3Q19, with top line results due by year end or early 2020.**
- **Results from a separate 'Window of Opportunity' study in various solid tumors showed that VX15 increased infiltration of killer T cells and reduced immunosuppressive activity in the tumors. This is important confirmation in patients of a finding previously reported in animal models.**
- **The unique properties of VX15 are also being evaluated in a potentially pivotal Phase 2 study in Huntington's disease, a devastating, progressive neurodegenerative disease. Top line data will be ready for submission to FDA in Q4 2020.**
- **Thirty thousand US patients are symptomatic with this genetic disease, and another 150,000 are at risk. One analyst puts the addressable market at $2.8 billion.**
- **VX15 is a humanized monoclonal antibody developed by Vaccinex. It binds and blocks the signaling activity of SEMA4D, a molecule that regulates the movement of immune and inflammatory cells to sites of injury, cancer or infection. Vaccinex is purposing it for high value applications in oncology and neurodegenerative diseases. For more on the science, go to www.vaccinex.com.**

Vaccinex, Inc.
(Nasdaq: VCNX)

Recent Price:	**$6.45**
Shares O/S:	**11.5 Million**
Approx. Mkt Cap:	**$74 Million**
Fiscal Year Ends:	**Dec. 31**

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Lung Cancer Phase 2

A 56-patient Phase 2 clinical trial of VX15 in advanced non-small cell lung cancer (NSCLC) is currently underway in collaboration with Merck KGaA, the European Merck.

The purpose is to determine if VX15 in combination with Bavencio, a Merck/Pfizer checkpoint inhibitor, performs better than Bavencio alone.

Enrollment in the open-label, two arm study is nearing completion.

Cohort A completed enrollment of 29 patients who have never been treated with checkpoint immunotherapy. Typically, their only prior treatment would have been chemotherapy which failed.

Cohort B will enroll 33 patients who failed immunotherapy with a single-agent checkpoint inhibitor such as Merck's Keytruda® or Bristol-Myers Squibb's Opdivio®.

Positive results will add to the growing body of evidence that suggests VX15 holds the potential to make checkpoint immunotherapy more effective for many more patients than is currently the case – *see Hot, Cold & Between.*

In data reported so far, the combination of VX15 and Bavencio has been well tolerated with toxicities essentially the same with the VX15-Bavencio combination as for Bavencio alone.

Melanoma Phase 2

Vaccinex expects to begin releasing top-line data early next year from a second open-label cancer study, this one in advanced melanoma patients whose tumors progressed after treatment with single agent immunotherapy.

The study is being conducted at UCLA in collaboration with Bristol-Myers Squibb, which is supplying two of its checkpoint inhibitors, Yervoy® and Opdivo.

The 36-patient Phase 2 trial consists of two cohorts of 18 patients each. One cohort will receive VX15 in combination with Yervoy, the other VX15 in combination with Opdivo.

The purpose of the study is to determine which combination is the most effective.

Top-line results are expected mid-2020.

Huntington's Disease Phase 2

VX15 has received Orphan Drug and Fast Track designations for Huntington's disease from the FDA. There is currently no FDA-approved disease-modifying treatment for the disease.

The current randomized, double blind placebo-controlled Phase 2 trial of VX15 in Huntington's disease has an adaptive design structure and includes three cohorts of which the latter two are potentially pivotal trials for registration.

Cohort A is completed. It enrolled 36 Huntington's disease patients randomized 1-1 drug to placebo. The randomized trial duration was six months.

Although changes in cognition and

Upcoming Events

3Q19 - Ph 2 additional data in NSCLC

2H19 - Publication of early HD data

1Q20 - Ph 2 Top line in NSCLC

1Q20 - Ph 2 Early data in melanoma

Mid-2020 - Ph 2 Top line in melanoma

2Q20 - Ph 2 in HD completed

4Q20 - Ph 2 Top line in HD

About Huntington's Disease

Huntington's disease is caused by a mutation in a single gene that's a dominant mutation. This means that when one parent has the disease, every child is at 50 percent risk because you only need to inherit one copy of the gene to get the disease. If a child has the mutation, they essentially have a 100 percent probability of getting the disease.

The disease takes decades for symptoms to emerge. It progresses slowly, and typically becomes manifest between the ages of 30 to 50 years, and then it becomes catastrophic.

One of the first symptoms to manifest is loss of motor control of arms and legs. Most often that's the least of the problems. Much more serious are the cognitive and psychological effects of the disease, which lead to long-term deterioration and degeneration of the brain and ultimately death.

The biology behind VX15's ability to potentially treat or prevent the symptoms of Huntington's disease is as complex as its intended result may seem simple.

The goal of treatment with VX15 is to minimize or prevent the transition to an inflammatory state and shutting down of normal functions of glial cells in the brain, most notably astrocytes, which occurs as Huntington's disease progresses.

Left untreated, Huntington's disease cripples the ability of astrocytes to do their job through a series of cascading inflammatory events which cause non-recoverable damage, killing off ever-expanding regions of the brain due to lack of nutrition and neuronal communication.

By downregulating inflammation, Vaccinex believes VX15 holds the potential to change the course of disease progression.

motor activity were measured, the main purpose was to detect changes in glucose uptake in the brain. This was important because, in their normal functional state, astrocytes play an important role in glucose transport. In contrast, when they undergo an inflammatory transition, they downregulate glucose transport and abandon this function.

If VX15 is effective in preventing the change associated with inflammation, then this should be reflected in glucose transport.

Happily, there are well-established methods available to measure changes in glucose uptake in the brain. The hoped-for outcome, therefore, was to document decreases in the decline of glucose uptake, or possibly an increase.

The results showed VX15 had a profound effect on glucose uptake in almost all brain regions, particularly in the frontal lobe and adjacent regions of the cortex, which are known to be greatly affected by Huntington's disease.

In most of the regions, metabolic activity increased between 5 percent and 20 percent after only six months of treatment. This was a relatively small trial. Nonetheless, it is the first instance of anyone reporting this kind of positive result for an intervention in Huntington's disease or any other neurodegenerative disease.

Cohort B is enrolling a total of 265 patients in two cohorts randomized 1-1 drug to placebo.

Cohort B1 includes 179 patients who've been diagnosed with Huntington's disease. Endpoints include VX15's impact on cognition, motor activity, other functional measures, and glucose uptake.

Cohort B2 includes 86 patients who are known to have the mutation but have not yet been diagnosed with Huntington's disease. They're known as premanifest or prodromal patients. The goal here is to see whether VX15 treatment can slow or prevent the onset of clinical symptoms, potentially expanding VX15's label.

Top-line data expected in 4Q20.

Hot, Cold & Between

Checkpoint inhibitors are clearly one of the fastest growing cancer therapies, with some analysts estimating the market will grow to more than $50 billion over the next five years.

But how well they work as single agents – or if they work at all – is highly dependent on the immune status of the tumor's microenvironment.

In lay terms, a tumor's immune status falls into three basic categories: hot, cold and lukewarm.

A tumor is hot when killer T cells have already penetrated the microenvironment and are trying feverishly to kill the tumor –but mostly they have difficulty because the tumor has checkpoint molecules that block the activity of killer T cells. Checkpoint inhibitors, like Keytruda and Opdivo, block the checkpoints and allow the T cells to do their work.

So, in the case of a hot tumor, checkpoint inhibitors can be successful as single agents, marshalling the enormous power of the body's own immune system. But naturally hot tumors are found in only roughly 20 percent of patients with certain types of cancer.

Cold tumors are cold because the patient has a paucity of killer T cells. For some reason, none or very few are available to attack the tumor. Without killer T cells, checkpoint technology is of little or no value.

The balance of the tumors falls into the lukewarm category, somewhere between hot and cold. Lukewarm tumors are tumors where there is an abundance of killer T cells hovering nearby the tumor, but they are blocked from getting in. They are stuck at the tumor boundary.

Patients with lukewarm tumors are the ones who may benefit most immediately from VX15 because it is designed to open the cellular gates of a tumor to allow killer T cells in, perfecting the microenvironment for checkpoint technology. VX15 has also been shown to suppress immune agents that down regulate cytotoxic activity, an added enhancement.

Summary

- **Vaccinex is conducting mid-stage clinical trials in advanced NSCLC, and melanoma, and a potential registration trial in Huntington's disease.**
- **Interim data from the Phase 2 in NSCLC was presented June 1, 2019 at ASCO, showing 63 percent of patients (10/16) had stable disease or shrinking tumor after failing single-agent checkpoint blockade therapy, mainly Keytruda. Five of the patients have been on study drug for four months or longer.**
- **Initial Phase 2 data from a collaborative study with Bristol-Myers Squibb in melanoma is expected in 1Q20, adding results with two more checkpoint inhibitors.**
- **The Phase 2 trial in Huntington's disease in on track to complete in 2Q20, with top-line data expected 4Q20.**
- **Vaccinex has 37 granted patents and 28 pending patents in the US and EU.**
- **Vaccinex cash and cash equivalents totaled $11.3 million at March 31, 2019.**

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