at a glance™

CHECKPOINT THERAPEUTICS

Upcoming: ***Interim data is expected later this month on roughly 50 percent of the patients enrolled in a potentially pivotal trial of Checkpoint's lead candidate, cosibelimab, in cutaneous squamous cell carcinoma (CSCC), the second most deadly form of skin cancer. Data reported at last year's ESMO Congress showed an overall response rate (ORR) of 50 percent with better than expected tolerability, suggesting the potential of a best-in-class entry in the $25 billion checkpoint inhibitor market now dominated by Merck's Keytruda®. Also in the pipeline: a novel small molecule for patients who cannot tolerate the side effects of Tagrisso®, a $4 billion AstraZeneca drug for lung cancer.***

Key Considerations

- **Checkpoint is one of eleven biopharma/ medical companies founded by Fortress Biotech (Nasdaq: FBIO).**
- **Checkpoint's lead candidate, cosibelimab, belongs to a $25 billion class of drugs called checkpoint inhibitors – the biggest selling of which are Merck's Keytruda and Bristol-Myers Squibb's Opdivo®.**
- **On January 13, 2020, Checkpoint announced that the FDA confirmed the company's plan to submit cosibelimab (*ko-see-bell-a-mab*) for full approval as a treatment for metastatic cutaneous squamous cell carcinoma (CSCC) based on safety and efficacy data from the ongoing 75-patient open-label, multi-center Phase 1 clinical trial.**
- **The first data report (14 patients) occurred at last year's ESMO Congress, showing an ORR of 50 percent compared to package insert ORRs of 47 percent and 34 percent, respectively, for Libtayo® and Keytruda, the two currently approved CSCC immuno-oncology agents.**
- **The next data set, to be reported this month, will cover roughly half the scheduled number of patients. If the data trends along the lines of what's been reported, it would further validate cosibelimab's differentiated features, including better tolerability.**
- **The next planned indication for cosibelimab is non-small cell lung cancer (NSCLC), the most common form of lung cancer, and by far the largest current indication for Merck's roughly $13 billion in Keytruda sales.**
- **Checkpoint expects cosibelimab to grab market share quickly through disruptive pricing in a $25 billion-dollar market where drugs are currently priced at $150K or more for a year of therapy.**
- **The company's second lead compound, CK-101, is being developed to address key deficiencies of AstraZeneca's blockbuster lung cancer drug, Tagrisso® – currently selling at an annualized rate of roughly $4 billion.**
- **Checkpoint recently reported $27 million in cash.**

Checkpoint Therapeutics, Inc.

(Nasdaq: CKPT)

Recent Price:	**$3.00**
Shares O/S:	**59 Million**
Approx MktCap:	**$177 Million**
Fiscal Year Ends:	**Dec. 31**

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Overview

Multi-billion-dollar-a-year drugs usually remain blockbusters until their patents expire – unless someone comes up with a better mousetrap. And if they do, they don't need a big share of a billion-dollar plus market to have a good business.

One way of doing this is to develop a lower cost alternative to the blockbuster – an especially viable and noble strategy these days when big drug companies often charge $150K or more a year for their blockbuster drugs.

Another way is to capitalize on a blockbuster's weak points – unacceptable side effects among certain users, for example.

These 'warm spots in a hot kitchen' strategies underpin Checkpoint's business and technical programs and define its portfolio of immuno-oncology agents and targeted drugs.

Checkpoint's anti-PD-L1 monoclonal antibody cosibelimab (CK-301) is being developed as a potentially better and lower-cost alternative in the fast growing $25 billion checkpoint inhibitor immuno-oncology market, now dominated by Merck's Keytruda and a handful of others.

Cosibelimab interim data has shown efficacy on par with the current first line checkpoint therapies in CSCC and NSCLC and, if current trends continue, it may prove to be safer with a more durable therapeutic effect.

Checkpoint's second compound, a tumor-targeted agent, is CK-101 for lung cancer, specifically designed for potentially better safety and at least as good efficacy as AstraZeneca's Tagrisso, currently on its way to $8 billion in annual sales, according to analysts.

Roughly 13 percent of Tagrisso users discontinue therapy due to side effects – a roughly $1 billion slice of the market Checkpoint hopes to serve with an equally effective, but safer alternative. Interim data suggests CK-101 can meet those objectives.

Checkpoint has a collaboration with TG Therapeutics (Nasdaq: TGTX) under which TGTX is developing cosibelimab in liquid tumors. Checkpoint is eligible for royalties and milestone payments from TGTX with their success.

Checkpoint I-O Program

Cosibelimab (CK-301), a potentially best-in-class anti-PD-L1 agent, was in-licensed from the Dana Farber Cancer Institute.

Notable & Upcoming

1Q20-FDA confirmed plan to submit cosibelimab (CK-301) for full approval in CSCC upon successful completion of ongoing Phase 1 trial

3Q20-Interim data expected from ongoing trial of cosibelimab in CSCC

Mid-2021-Topline full dataset from cosibelimab in CSCC

2021-Possible start of Ph 3 registration trial of cosibelimab in NSCLC with EGFR mutations

YE-2021-Possible start of Ph 3 registration trial of CK-101 in NSCLC with EGFR mutations

2021-Planned filing for FDA approval of cosibelimab (CK-301) in CSCC

It belongs to a proven class of molecules known as checkpoint inhibitors, for which Checkpoint Therapeutics is named.

Just like the first six PD-1 and PD-L1 checkpoint inhibitors (Opdivo, Keytruda, Libtayo, Tecentriq®, Bavencio®, and Imfinzi®), Checkpoint's candidate enables native killer T cells to attack cancer cells by unblocking one of the tumor's main defense mechanisms.

I-O Leader Board - CSCC

	ORR %	
Libtayo	47	(pkg insert)
Keytruda	34	(pkg insert)
Cosibelimab	50	(2019 ESMO)

In the case of cosibelimab, the unblocking is accomplished by binding to the ligand PD-L1, the tumor's protective shield, allowing killer T cells to 'see' and attack the previously hidden tumor cells.

But it may be doing more. Interim data released at scientific symposia in May and September 2019 revealed that cosibelimab, unlike currently marketed checkpoint inhibitors, has a half-life that supports sustained high (greater than 99 percent) tumor target occupancy to unleash the killer T cells, with the added benefit of also pulling in the natural killer cells of the immune system for potential enhanced efficacy in certain cancers.

This especially strong activity may provide greater cancer killing power than currently approved PD-1 and PD-L1 inhibitors.

In the latest interim data, released September 30, 2019 at ESMO (largest oncology conference in Europe), cosibelimab achieved an ORR of 50 percent in metastatic CSCC, essentially the same as the 47 percent ORR achieved in separate studies of Libtayo, the first immuno-oncology agent approved for this indication.

In June of this year, Keytruda become the second FDA-approved checkpoint inhibitor in metastatic CSCC with an ORR of 34 percent, creating a new and lower benchmark for approval in this indication.

Cosibelimab's performance vs. Keytruda's has drawn promising attention in another indication, NSCLC -- Keytruda's biggest indication at roughly $11 billion annually. Cosibelimab's 2019 ESMO readout showed a 40 percent ORR with 6 percent Grade 3 or higher treatment-related adverse events vs. Keytruda's package insert ORR of 39 percent, with 27 percent Grade 3 or higher AEs (*New England Journal of Medicine*).

Based on the quality and strength of interim data, especially in CSCC, cosibelimab's Phase 1 trial transitioned into a potentially pivotal trial in January 2020 based on discussions with the FDA.

The study is on track to announce updated interim data (roughly 35 patients) at this year's ESMO (September) with the full pivotal dataset in CSCC expected mid-2021.

The primary endpoint will be ORR, the same endpoint that led to the approvals of Libtayo and Keytruda in CSCC – a large $1 billion+ market with roughly 7,000 deaths annually in the US alone.

The timing of the cosibelimab trial in CSCC suggests that a filing for approval (a Biologics License Application, or BLA) with the FDA could occur before the end of 2021.

Today, there are literally hundreds of clinical trials underway at scores of company, university and government labs teaming approved checkpoint inhibitors with tumor-targeted agents in the quest for more durable remission rates. Analysts predict combination therapies will drive the checkpoint inhibitor market to $50 billion in five years.

While side effects are important with any drug – especially if they are treatment limiting – they take on added importance when two or more drugs are combined. This puts a special spotlight on cosibelimab's 6 percent Grade 3 or higher treatment-related AE readout (ESMO '19) compared to Keytruda's 27 percent Grade 3 or higher AEs (*New England Journal of Medicine*). The lower the toxicity of each component of a combo drug, the lower the combination's overall toxicity will likely be unless they are contraindicated. If cosibelimab maintains its low toxicity profile through final data, it could become a checkpoint inhibitor of choice for combo therapies.

Tumor-Targeted Agent CK-101

Checkpoint's third generation EGFR (epidermal growth factor receptor) inhibitor is currently in a Phase 1 clinical trial in non-small cell lung cancer (NSCLC).

The first two generations of EGFR inhibitor drugs showed strong performance in NSCLC but they only work for about 10 months, on average, due to tumors forming resistance. Third generation EGFR inhibitors prevent this initial resistance, leading to much longer benefit.

The first third-generation EGFR inhibitor (Tagrisso [AstraZeneca] initially approved as second line therapy in 2015 and then as first line in 2018) works very well in NSCLC patients, but 13 percent of the patients experience significant cardiovascular, lung, skin or other toxicities, causing them to discontinue Tagrisso therapy.

Encouraging safety and efficacy data from the ongoing Phase 1 trial of CK-101 was last reported September 24, 2018 at the International Association for the Study of Lung Cancer World Conference in Toronto. The data showed CK-101 to be efficacious against NSCLC with EGFR mutations, with a potentially differentiated safety profile versus Tagrisso.

Key data highlights from the CK-101 trial so far include 100 percent disease control rate (stable disease or better), 84 percent of patients with tumor lesion reductions, a 53 percent overall response rate and no treatment-limiting side effects reported.

Additional data is being evaluated to decide the optimal dose for a Phase 3 registration trial expected to start in 2021 in 1st line (treatment-naïve) EGFR mutant NSCLC patients.

The Phase 3's primary endpoint will be progression free survival—the same basis on which Tagrisso was approved.

But the differentiated safety profile shown so far by CK-101 will be the key to a strong market entry, first addressing the 13 percent of EGFR mutant NSCLC patients who discontinue Tagrisso therapy, and then the broader population, since there is no test to tell in advance who will suffer Tagrisso's side effects.

In a word, Checkpoint could capture a sizable piece of what is projected to become a $8 billion market in the next five years, up from roughly $4 billion today.

Summary

- **Checkpoint's cosibelimab (CK-301), an anti-PD-L1 checkpoint inhibitor, is being developed as a potentially better and lower cost alternative to current therapies in the $25 billion checkpoint market.**
- **With pivotal cosibelimab data expected mid-2021, Checkpoint should soon be viewed as a 'near-term revenue opportunity', highly sought after by large biotech and pharma.**
- **Multiple disease indications are potentially addressable by single agent cosibelimab, as has been the case with other drugs in the class. Its trending efficacy and safety attributes may also make it a drug partner of choice in combination immuno-therapies.**
- **The company's second lead candidate, CK-101, is aimed at the current $4 billion (and growing) annual market AstraZeneca created with Tagrisso for EGFR mutant lung cancer patients.**
- **Cash and cash equivalents stood at $27 million at June 30, 2020.**

For additional information, contact:

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