Checkpoint Therapeutics’ strategy is to develop combination cancer therapies at the cutting edge, to empower the body’s immune system to kill cancer cells in conjunction with tumor targeted agents. The company’s lead tumor targeted agent, CK-101, holds the potential of providing a safer alternative to AstraZeneca’s $1 billion+ drug Tagrisso® for EGFR mutant non-small cell lung cancer patients who fail first line therapy. A Phase 2 trial is scheduled to start 1Q18.

**Key Considerations**

- **Checkpoint is one of nine biopharmaceutical companies majority controlled by Fortress Biotech (FBIO).**
- **Checkpoint raised $58 million in private capital and went public 4Q16.** The company up-listed and shares began trading on Nasdaq June 26, 2017.
- **The company’s business strategy is to develop agents to heighten the cancer-killing power of the body’s immune system (in 2 ways), and to develop tumor targeted anti-cancer agents for use as monotherapy and in combination with its immune system agents.**
- **This drug combination strategy (using immune system enhancers or so-called immuno-oncology ‘I-O’ therapy together with tumor targeted agents) represents the leading edge of promising new treatments for a rapidly growing list of solid and blood-born cancers.**
- **Checkpoint has three lead programs: two I-O agents, and one targeted agent in lung cancer (CK-101) specifically designed for a potentially better safety profile and at least as good efficacy as Astra Zeneca’s Tagrisso.**
- **By developing both components of a combination therapy – the I-O agent(s) and the tumor-targeted drug – Checkpoint will have the ability, unlike most innovators, to competitively price the combination. Its proprietary drug combinations won’t require use of another company’s product over which it would have no pricing control.**
- **Checkpoint has a collaboration with TG Therapeutics (Nasdaq: TGTX) under which they will jointly develop the Anti-PD-L1, Anti-GITR, and BET inhibitor programs – Checkpoint in solid tumors and TG in liquid tumors. Checkpoint is eligible for royalties and milestone payments.**

**Checkpoint Therapeutics, Inc.**

(Nasdaq: CKPT)

Recent Price: $8.05  
Shares O/S: 25 Million  
Fiscal Year Ends: Dec. 31  
Published: September 2017

This could be a competitive disadvantage. A Phase 1 study for Checkpoint’s anti-PD-L1 candidate is planned to commence 3Q17. Pre-clinical data leads the company to believe its PD-L1 inhibitor has strong activity, and may, in fact, have greater cancer killing power than currently approved PD-1 and PD-L1 inhibitors owing to its retention of native features of the antibody.

**Checkpoint I-O Program**

Checkpoint in-licensed two immuno-oncology (I-O) candidates from Dana-Farber Cancer Institute:

- The lead I-O candidate is an anti-PD-L1 agent, referred to as CK-301. It belongs to a proven class of molecules known as checkpoint inhibitors, for which Checkpoint Therapeutics is named. Just like the five currently approved PD-1 and PD-L1 checkpoint inhibitors (Bristol-Myers Squibb’s Opdivo®, Merck & Co’s Keytruda®, Roche’s Tecentriq®, Pfizer/Merck KGaA (Bavancio®, and Astra Zeneca (Imfinzi®), Checkpoint’s candidate also is designed to enable native T Cells to attack cancer cells by unblocking one of the tumor’s main defenses against them.
- The unblocking is accomplished by disabling the ligand PD-L1, the tumor’s protective shield. This allows T Cells to ‘see’ the previously hidden tumor cells and launch an attack.
- The developers of the five marketed checkpoint inhibitors all followed the same course: to first get their drugs approved as monotherapies. Now their attention, and the attention of scores of other companies, has turned to testing how these I-O drugs can be therapeutically linked to other I-O and tumor targeted drugs for a synergistic attack on the cancer.
- If you own both components of a combo (like Checkpoint will) you’re in good shape. But many of the innovators working in this area own only the tumor targeted component, which means the combined pricing of their drug and another company’s I-O agent is not completely in their control.

**Notable & Upcoming**

- **3Q17 - Target start of first I-O agent Phase 1 study**
- **3Q17 - FDA grants Orphan Drug designation for CK-101 in EGFR mutation-positive non-small cell lung cancer**
- **1Q18 - Expected start of CK-101 Phase 2 in lung cancer**
- **1Q18 - Target for IND filing for CK-103 (BET inhibitor)**
- **1H18 - Potential clinical data updates from CK-101 and CK-301 clinical trials**
- **$27 Million - Cash/ equivalents at 6/30/17**
IND-enabling studies for the anti-GITR candidate started 4Q16, with an IND filing anticipated in 2018.

Both I-O candidates are seen as widely applicable among many tumor types, particularly in solid tumors. The expectation is the two would be used in combination with one another: anti-PD-L1 to enable T Cells, and anti-GITR to boost their effectiveness. If approved, the two together could address a projected $30 billion+ global market opportunity in I-O therapy.

Both Checkpoint I-O candidates will initially be tested as monotherapies, then in combination with each other and Checkpoint’s tumor targeted agents.

**TUMOR TARGETED AGENTS**

Checkpoint’s tumor targeted cancer therapy portfolio currently includes four candidates, each providing unique mechanisms to target and kill cancer cells.

**CK-101** –This third generation EGFR (epidermal growth factor receptor) inhibitor is currently in a Phase 1/2 clinical trial and is under development for the treatment of patients with non-small cell lung cancer (NSCLC). If Checkpoint’s clinical trials are successful, it expects CK-101 would initially be prescribed as monotherapy in T790M mutation-positive NSCLC patients, then later in combination with one or both of its I-O agents. Pre-clinical studies of CK-101 showed strong dose-dependent activity against T790M mutation positive NSCLC and substantially (100 fold) lower affinity for wild-type (normal) EGFR.

After 12-14 months of first line therapy (typically Tarceva®-Genentech) approximately 60 percent of NSCLC patients will develop drug resistance due to the T790M mutation. These individuals can be identified with a diagnostic sold by Roche, enabling Checkpoint to offer CK-101 as a precision medicine.

The current Phase 1/2 dose escalating trial of CK-101 commenced in September 2016. It will enroll approximately 30 advanced solid tumor patients. The study will determine the maximum tolerated dose and the recommended Phase 2 dose.

Positive preclinical studies that preceded the Phase 1/2 initiation were reported 2Q17 at the American Association for Cancer Research (AACR) Annual Meeting, strongly supporting the clinical development program underway.

The currently planned Phase 2 trial is expected to commence 1Q18, enrolling approximately 60 NSCLC patients identified as being T790M mutation positive by the Roche diagnostic. The expected protocol and primary endpoint (Objective Response Rate [ORR]) are the same used for accelerated FDA-approval of Tagrisso based on Phase 2 data. The addressable market is estimated at $3 billion+.

**CK-102** –PARP is an enzyme that is essential in the repair of DNA. CK-102 is designed to inhibit PARP, preventing certain cancer cells from repairing the DNA damage done by anti-cancer agents. Certain cancers, especially BRCA mutant types, are more sensitive than others to PARP inhibitors.

PARP inhibitors as a class have shown promising activity in multiple cancers such as breast, ovarian, and prostate, and particularly in tumors with existing defects in BRCA1 and BRCA2.

The importance and promise of PARP inhibitors was underscored by the 2016 acquisition of Medivation by Pfizer for $14 billion, largely due to Medication’s PARP agent (talazoparib).

CK-102 underwent a Phase 1 dose escalation study before Checkpoint licensed the compound from Teva Pharmaceuticals. Checkpoint is currently planning the next steps in the clinical development program for CK-102. The addressable market is estimated at $1 billion+.

**CK-103** –This is an oral small molecule inhibitor of BRD4, a BET protein, which is known to promote the activity of the c-Myc oncogene. Research by others has implicated certain BET genes in the pathogenesis of acute myeloid leukemia, multiple myeloma, and acute lymphoblastic leukemia and the sensitivity of these cancers to BET inhibitors. CK-103 is currently in pre-clinical development. Checkpoint expects to start clinical trials of CK-103 in 1H18.

Anti-CAIX (CA-9) –Licensed from Dana-Farber, this is a fully human antibody engineered to treat hypoxia-induced CAIX+ renal cell carcinoma and other CAIX+ tumors.

It has been specially engineered to enhance antibody-dependent cell-mediated cytotoxicity (ADCC), an immune system defense mechanism in which certain killer cells actively penetrate a targeted diseased cell whose membrane-surface antigens have been bound by specific antibodies. The candidate is in pre-clinical development.

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**SUMMARY POINTS**

- Checkpoint Therapeutics has technology-leading programs including immuno-oncology (I-O) agents and tumor targeted cancer drugs, the two components of ‘new-wave’ combination therapies.
- Because Checkpoint is the innovator of both components of its planned combination therapies, it can maintain control over the pricing of the total combination.
- Checkpoint’s first I-O candidate is expected to enter the clinic 3Q17 as a potentially new addition to a proven class of I-O agents, PD-L1 inhibitors, which enable native T Cells to attack cancer tumors.
- Its first tumor targeted candidate is aimed at the $1 billion+ (and growing) market AstraZeneca created by the launch of Tagrisso for EGFR T790M positive lung cancer patients. Checkpoint’s candidate, CK-101, has been engineered to potentially avoid the treatment limiting skin toxicity of Tagrisso. A Phase 2 trial is scheduled to start 1Q18.
- Look for news of clinical trial starts as the year progresses. Initial clinical results due 1H18.
- Cash and cash equivalents stood at $27 million at June 30, 2017.

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