at a glance™

FORTRESS BIOTECH

Upcoming anticipated milestones at Fortress partner companies: initiation of a rolling New Drug Application (NDA) in 2H21 for Menkes disease, a rare pediatric disorder that kills many of those afflicted before age three, followed by release of topline results from a registration-enabling trial of cosibelimab, a checkpoint inhibitor designed to rival Keytruda® and Libtayo® in two important cancers. Other anticipated milestones include the start of several pivotal clinical trials, Phase 1 and Phase 2 readouts, and potential buyouts of two Fortress partner companies under existing option/contingent acquisition.

Key Considerations

•Biotech/biopharma investors seeking a risk-balanced vehicle that spans multiple therapeutic categories may be hard pressed to look further than Fortress Biotech.

•The company's global reach in finding and in-licensing promising drug development programs has created a portfolio of seven marketed drugs and over 25 preclinical to late-stage candidates in multiple therapeutic categories.

•Fortress creates individual companies as the most efficient and least dilutive way to clinically advance early-stage drug development programs identified and in-licensed by its team of more than 10 business developers.

•Eleven companies have been formed so far. Fortress' ownership in each currently ranges from 20 to 93 percent.

•Two key events expected this year are the submission of a rolling NDA for marketing approval in Menkes disease, and release of topline line data from a registration-enabling trial of a new anti-PD-L1 checkpoint inhibitor.

•The candidate for Menkes disease, a rare genetic disorder, increased survival nearly 80 percent to 14.8 years, according to findings of a recently completed topline efficacy analysis.

•The latest interim data reported for the checkpoint inhibitor cosibelimab *(ko-see-bell-a-mab)* shows comparable or higher overall response rates and more favorable safety than Keytruda in two important cancers so far.

•Fortress partner company Checkpoint Therapeutics expects cosibelimab to grab market share quickly through disruptive pricing in a $25 billion market (predicted to double in five years) where drugs are currently priced at $150K or more for a year of therapy.

Fortress Biotech, Inc.
(Nasdaq: FBIO)

Recent Price:	**$4.11**
Shares O/S:	**97 Million**
Approx. Mkt Cap:	**$399 Million**
Fiscal Year Ends:	**Dec. 31**

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This edition of Fortress At A Glance focuses on two of the company's most advanced programs.

Copper Deficiency in Newborns Many Die Before Age 3

In the second half of this year, Fortress partner company Cyprium Therapeutics (72 percent owned) plans to initiate a rolling submission of New Drug Application (NDA) for FDA marketing approval of copper histidinate (CUTX-101) for the treatment of Menkes disease, an X-linked recessive copper metabolism disorder caused by mutations in ATP7A gene, an evolutionary conserved copper transporting ATPase.

It is a rare genetic pediatric disorder for which there is currently no approved treatment. Left untreated, few born with Menkes disease survive beyond age three.

Babies born with Menkes disease have low levels of copper in their blood and brain, as well as abnormal levels of certain neurochemicals. Diagnosis is made by sequencing the ATP7A gene.

Menkes disease and related copper disorders are characterized by distinctive clinical symptoms such as sparse and depigmented hair (kinky hair), connective tissue problems and severe neurological symptoms, such as seizures, developmental delays, and failure to thrive.

In the recently reported topline efficacy analysis of CUTX-101 in early treated Menkes disease patients, CUTX-101 showed a nearly 80 percent reduction in the risk of death (Hazard Ratio = 0.21. $p<0.0001$) compared to an untreated historical control.

Median survival in the early treatment cohort was 14.8 years (177.1 months) compared to 1.3 years (15.9 months) for the untreated historical control cohort.

CUTX-101 has been granted Fast Track, Breakthrough Therapy and Rare Pediatric Disease designations by the FDA for Menkes disease.

The FDA also granted Orphan Drug designation to CUTX-101 and AAV-ATP7A, a preclinical gene therapy to treat Menkes. In July 2020, the European Medicines Agency Committee for Orphan Medicinal Products issued a positive opinion on an application for Orphan Drug Designation of CUTX-101.

The minimum US birth prevalence for Menkes disease is believed to be 1 in 34,810 males, and potentially as high as 1 in 8,664 live male births when missense variants of ATP7A are included, based on recently updated genome-based statistics in the Genome Aggregation Database.

Methods to detect Menkes disease at birth are improving. Details of a next generation newborn screening test were published last summer in Molecular Genetics and Metabolism Reports, assessing its analytic validity as a potential newborn screen of Menkes disease.

LATE NEWS: In February 2021 Cyprium entered into a development and asset purchase agreement with Sentynl Therapeutics. Under the terms, Cyprium is eligible to receive up to $20 million in upfront and regulatory cash milestones through NDA approval, potential sales milestones totaling up to $255 million, and royalties on CUTX-101 net sales ranging from 6 percent on that portion of net sales below $75 million, up to 25 percent on that portion of net sales above $100 million. Cyprium will retain 100 percent ownership of any FDA priority review voucher that may be issued in connection with NDA approval of CUTX-101.

Priority review vouchers, which can be redeemed to receive FDA priority review of a subsequent marketing application for

a different product are transferrable, with current prices in the $100 million range.

The voucher program may also be available to another development program at a Fortress partner company, a treatment for Bubble Boy disease (XSCID).

In keeping with a basic Fortress strategy to fund R&D at the partner company level, Cyprium raised net proceeds of approximately $7.1 million in September 2020 in a private placement of 9.375 percent Series A Cumulative Redeemable Perpetual Preferred Stock.

Keytruda-Like Candidate in $25B Market

Fortress partner company Checkpoint Therapeutics (Nasdaq: CKPT--21 percent owned by FBIO) is developing cosibelimab (CK-301), a potentially best-in-class anti-PD-L1 checkpoint inhibitor in-licensed from the Dana Farber Cancer Institute.

Cosibelimab is in clinical trials for two lead indications, metastatic cutaneous squamous carcinoma (mCSCC) and Non-Small Cell Lung Cancer, or NSCLC.

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.

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.

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

Interim data released September 17, 2020 at the European Society for Medical Oncology (ESMO) Virtual Congress 2020 (largest oncology conference in Europe) showed cosibelimab achieved an Overall Response Rate, or ORR, of 51.4 percent in mCSCC, essentially the same as the 47 percent ORR achieved in separate studies of Libtayo, the first immuno-oncology agent approved for this indication.

Immuno-oncology Leader Board in mCSCC

	ORR (%)	
Libtayo	*47*	*(package insert)*
Keytruda	*34*	*(package insert)*
Cosibelimab	*51*	*(interim data 2020 ESMO)*

In June 2020, Keytruda become the second FDA approved checkpoint inhibitor in mCSCC with an ORR of 34 percent, creating a new and lower benchmark for approval in this indication.

Topline results from the on-going study of cosibelimab in mCSCC are expected 2H21 and, if positive, would put cosibelimab on track for filing a Biologics License Application, or BLA, with the FDA in 1H22. If the BLA is approved, cosibelimab could be on the market in 1H23.

The primary endpoint in mCSCC will be ORR, the same endpoint that led to the approvals of Libtayo and Keytruda in mCSCC – a large $600 million market expected to grow to $1 billion+ with roughly 7,000 deaths annually in the US alone.

Cosibelimab's performance vs. Keytruda in mCSCC coupled with recent interim data in NSCLC has drawn promising attention to its potential in NSCLC -- Keytruda's biggest indication at roughly $11 billion in sales annually.

A Phase 1 cohort (25 patients) of cosibelimab in NSCLC presented at the Society for Immunotherapy of Cancer (SITC) 35th Anniversary Annual Meeting last November showed a 44 percent ORR, comparable to Keytruda's package insert ORR of 45 percent.

A Phase 3 registration-enabling trial is planned in first line metastatic NSCLC.

Safety is emerging as another key attribute of cosibelimab and, together with efficacy, could become one its defining features as immuno-oncology moves more towards combination therapies.

At the time of the most recent interim analysis (SITC 2020), 123 patients with advanced cancers had been treated with cosibelimab. The data shows cosibelimab appears to have a potentially favorable safety profile compared to anti-PD-1 therapies currently available.

Less than five percent of study patients reported Grade 3 or higher treatment-related Adverse Events compared to 27 percent Grade 3 or higher AEs reported for Keytruda (multiple indications) in the *New England Journal of Medicine*.

Hundreds of clinical trials are currently 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 lethal or treatment limiting – they take on added importance when two or more drugs are combined.

This puts a special spotlight on cosibelimab's currently reported safety profile.

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.

Other Late-Stage Programs

NDA Stage: IV Tramadol for postsurgical pain. Phase 3: CAEL-101 for Amyloid light chain amyloidosis. Pivotal Phase 2: MB-107 and MB-207 for newly diagnosed and previously transplanted Bubble Boy disease (XSCID); and Phase 2: CEVA-101 for pediatric and adult traumatic brain injury. Twenty plus other programs are in early clinical and preclinical stages. Visit www.fortressbiotech.com for full details.

Summary

- **Key partner company events expected in 2021 include initiation of a rolling NDA for a rare pediatric disorder in 2H21 (Menkes disease), and topline data in 2H from a registration-enabling trial of a new checkpoint inhibitor designed to initially rival Merck's Keytruda and Sanofi-Regeneron's Libtayo in two big cancer markets.**
- **The Menkes disease candidate is on track to become the first NDA filing of a treatment for a genetic disorder that kills many of those afflicted before the age of three – CUTX-101 has been shown to increase median survival time by nearly 80 percent to just over 14 years.**
- **Checkpoint inhibitor cosibelimab interim data shows comparable or higher ORR and more favorable safety than Keytruda in two important cancers so far.**
- **Fortress's majority-owned revenue-generating company, Journey Medical Corp., markets seven dermatology products and reported revenue for 1Q21 of $10.7 million.**
- **At March 31, 2021, Fortress reported consolidated cash, cash equivalents, and restricted cash of $291.5 million.**

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