at a glance™

Artelo BIOSCIENCES

Of Note: ***Artelo is developing a diverse portfolio of drug candidates that act upon the endocannabinoid system. A mid-stage program in cancer anorexia is due to produce initial data in 4Q21, with topline results from a Phase 2a efficacy study expected in 1H22. Estimates put the potential market in excess of several billion. Two preclinical programs are advancing with validated mechanisms.***

Key Considerations

- **Artelo's portfolio of three drugs candidates, while aimed at a diverse range of indications, share a common root: all are designed to alter activity of the endocannabinoid system, the body's 'master regulator' that harmonizes most key bodily organs.**
- **Near term milestones include expected topline results before year end from the dose ascending Phase 1b portion of a Phase 1b/2a clinical trial in cancer anorexia, followed by topline results from the 2a efficacy portion in 1H22.**
- **Analysts estimate the commercial market for a drug specifically indicated for cancer anorexia is $2 billion annually and could grow significantly with a new patented market entry.**
- **Artelo's two other candidates are preclinical.**
- **One is a small molecule candidate engineered to disrupt fatty acid metabolism (endocannabinoids are fatty acids and amides) within tumors to prevent their growth and metastasis.**
- **The other is a novel synthetic cocrystal of cannabidiol (CBD) and a common food additive with medicinal properties. It is being developed initially for post-traumatic stress disorder, or PTSD.**
- **Wall Street's interest in CBD-based drugs was highlighted earlier this year when Jazz Pharmaceuticals agreed to buy GW Pharmaceuticals, developers of Epidiolex®, the first (and so far only) FDA-approved CBD-based drug, for roughly $7 billion, mainly on the strength of its CBD-based revenue and pipeline.**

Overview

All three of Artelo's drug candidates share a common feature in that they are designed to alter signaling of the endocannabinoid system, including the G-protein-coupled cannabinoid receptors that dominate much of its activity.

Artelo Biosciences, Inc.
(Nasdaq: ARTL)

52 Week Range:	**$0.45-$3.67**
Shares O/S:	**24.5 Million**
Approx. Mkt Cap:	**$20 Million**
Fiscal Year Ends:	**August 31**

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Some scientists call the endocannabinoid system the 'master regulator' because of the abundance of cannabinoid receptors throughout the body and their influence on the body's ability to maintain equilibrium between the organ systems we rely on for metabolic functioning, sleep, mental acuity, and scores of other life-sustaining processes, some still to be defined.

One of challenges of developing drugs that target the endocannabinoid system is avoiding overactivation of receptors in the central nervous system (CNS) that may trigger unintended side effects, such as a feeling of euphoria that is associated with tetrahydrocannabinol (THC) in cannabis.

Artelo's drug candidates are engineered to minimize CNS side effects, and to target outcomes that could enhance the intended therapeutic benefit.

Hunger Without the High

There is an adage that says the fortunes of local Taco Bells rise and fall with the use of marijuana, highlighting the well-known correlation between cannabis and the munchies.

It would not be surprising therefore to theorize that sick people who are wasting away due to lack of appetite might consider cannabis to stimulate their hunger, but hesitate to use it due to potentially feeling less control of their life from the CNS effects.

The medical rationale behind that notion is the *raison 'de etre* for the development of ART27.13, a mid-stage drug program to treat cancer anorexia, a debilitating and often fatal condition that affects more than 60 percent of advanced cancer patients.

It is characterized by the uncontrolled wasting away of lean body mass due to lack of appetite. The onset is generally attributable to the effects of chemotherapy and the advancing morbidity of the cancerous state.

It is estimated that between three to five of every ten diagnosed cancer patients die of anorexia, not the cancer. Although it spares few forms of cancer, its prevalence is highest among prostate, gastric, and lung cancer patients.

In the absence of an FDA-approved treatment or standard of care, physicians tend to treat anorexia with a hit or miss mix of nutritional counseling, IV supplements, and appetite stimulants such as corticosteroids. Analysts believe the commercial market for an approved drug could exceed several billions.

ART27.13 was originally developed at AstraZeneca (AZ) and came to Artelo through a licensing agreement. AZ had been developing the compound as a pain medication, hoping to take market share from the likes of a Motrin® or Tylenol®.

Upcoming

-4Q21 – Initial results expected from first stage of Phase 1b/2a trial of lead compound ART27.13 in cancer anorexia

-1H22 – Topline efficacy data expected from Phase 2a randomized portion of same trial

-2H22 – Expected start of ART26.12 cancer trial with focus on prostate and breast cancer patients

After completing five Phase 1 clinical studies involving 205 participants, AZ concluded that the compound's analgesic properties were insufficient to warrant further development for a pain indication.

Hope springs eternal in many drug development programs, and the silver lining in this instance was the observation of an unintended dose-dependent weight gain among patients taking ART27.13.

A dose escalating trial over 12 days in patients with low back pain found an unexpected effect on body weight. Participants in the upper percentile of response gained about 3 percent of their baseline body weight during just 12 days of treatment and the slope of the weight gain curve versus the placebo subjects indicated significant differences among the participants (p=0.0001).

Because of the clinical data AZ generated, Artelo was able to move directly into dose optimization and efficacy trials for a potential indication in cancer anorexia.

Early Data Due 4Q21

In April of this year, Artelo initiated a Phase 1b/2a clinical study of ART27.13 called the Cancer Appetite Recovery Study (CAReS), a trial of approximately 45 advanced cancer patients with symptoms of anorexia.

Inclusion criteria include a documented five percent weight loss during the past six months and abstinence from any active cancer therapies during the 90-day trial period.

The Phase 1b stage, currently underway, plans to enroll 18 patients, with six patients in three dose escalation groups. Enrolled patients will receive 150, 250, or 400 µg (and an option to use 650 µg if needed) of ART27.13 orally once a day. The objective is to determine the optimal dose for the Phase 2a portion of CAReS.

The selected dose will be studied in the randomized, placebo-controlled Phase 2a efficacy portion of the trial with an expected enrollment of 25.

The primary efficacy endpoints for the Phase 2a include lean body mass, weight gain, and changes in quality of life.

Phase 1b data is expected 4Q21, with the results from the Phase 2a efficacy portion expected in 1H22.

It is instructive to note that AstraZeneca, while evaluating ART27.13 for pain, conducted dependency studies which suggested the compound is non-habit forming and had limited psychoactive effects.

The feature is most likely due to the way ART27.13 was engineered.

ART27.13's physiochemical properties combined with other attributes prevent it from materially breaching the blood brain barrier, limiting any potential triggering of euphoria. Heat maps from nuclear imaging brain scans of monkeys dosed with radiolabeled ART27.13 confirm this, as do clinical observations.

ART27.13 is also known to have higher impact for receptors in the gut region versus the brain because of where it is present. In the periphery it targets CB_1 and CB_2 receptors on the surface of the cells in the intestines, stomach, skeletal muscle, fatty tissue, and the liver.

Unlike THC it fully agonizes, or turns on, cannabinoid receptors, sending a 'feed me' signal to the brain which alters metabolic activity –a welcome message for a body wasting away from lack of appetite.

Artelo believes ART27.13 is the first and only full agonist of CB_1 and CB_2 to enter this stage of development with results expected in the near term.

Artelo Cancer Program

In cancer, Artelo is taking advantage of recent discoveries in the field of fatty acid binding proteins found in human cells. Artelo's focus currently is on number five, known as Fatty Acid Binding Protein 5, or FABP5. The program at Artelo is called ART26.12.

FABP5 is instrumental in mobilizing a gene called Vascular Endothelial Growth Factor or VEGF, which stimulates the growth of new blood vessels in tumors, enabling them to grow and metastasize. Disrupting VEGF is expected to hinder tumor growth and to prevent them from spreading.

The program was licensed from Stony Brook University (NY) which had support from the NIH of $3.8 million and more recently was awarded $4.2 million from the NCI to support advancing the science in prostate cancer.

Artelo plans to initiate Phase 1 clinical cancer trials in late 2022 or early 2023, with enrollment likely to trend to patients with prostate and breast cancers – the two tumor types it believes will support the most efficient regulatory strategy.

Expression of FABP5 is frequently higher in patients with aggressive tumors. Studies show that patients with high FABP5 have the worst prognosis.

Interestingly, bodily fluid levels of FABP5 can be measured non-invasively (breath or salvia) as a biomarker to identify those most likely to benefit from ART26.12. This could expedite clinical development and facilitate reimbursement should ART26.12 be approved.

CBD With A Patent!

There are many high incidence medical conditions drug developers feel could benefit greatly with CBD-based drugs.

The choke point has always been optimizing CBD as a solid formulation for the pharmaceutical markets and in highly prevalent indications.

GW Pharmaceuticals engineered its epilepsy drug Epidiolex for an orphan indication, earning a 7-year market exclusively package from the FDA under the Orphan Drug Act for its patented formulation.

For larger markets like anxiety, stroke, PTSD, sleep, or IBD, drug developers must address the inherent inconsistency of CBD and create a composition with improved drug-like properties. So doing would provide the potential of long-term patent protection and the prospects of strong market exclusivity.

Artelo believes it has solved this challenge with ART12.11, a novel cocrystal composition that combines CBD with tetramethylpyrazine (TMP), a coffee-flavored European Food Safety Authority approved food additive with medicinal and physical properties that may potentiate CBD efficacy when given in high doses.

Literature suggests that the two components of the cocrystal could benefit each other's bioavailability and Artelo is currently investigating this in preclinical studies. The cocrystal of CBD:TMP was awarded United States Patent Office composition of matter and use patents in 2020, providing commanding protection until the end of 2038.

The potential of addressing a broad range of indications with an enhanced and patented composition of CBD has already drawn attention from potential partners and large pharma companies.

Summary

- **Artelo is a leading developer of drugs designed to modulate the activity of the endocannabinoid system for a wide range of unmet needs, the most advanced of which is the treatment of cancer anorexia.**
- **Initial results of a Phase 1b/2a clinical trial of ART27.13 in cancer anorexia are due 4Q21, with topline results of the Phase 2a efficacy portion due 1H22.**
- **An earlier dose escalating study of the compound in the setting of lower back pain showed significant weight gain of up to 3 percent of baseline body weight after 12 days versus the participants on placebo (p=0.0001).**
- **The company expects to be in the clinic by the end of next year with its cancer candidate ART26.12, and it is investing in preclinical studies in order to bring its patented ART12.11 CBD cocrystal program to the clinic as soon as possible.**

For additional information, contact:

Redington, Inc. • CT 203 222-7399 • NY 212 926-1733 • www.redingtoninc.com

Artelo Biosciences, Inc. • 760 943-1689 • www.artelobio.com