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David Bautz, PhD
(312) 265-9471
dbautz@zacks.com

scr.zacks.com
10 S. Riverside Plaza, Chicago, IL 60606

Virios Therapeutics, Inc.

(VIRI-NASDAQ)

VIRI: Initiating Coverage of Virios Therapeutics; Attacking the Root Cause of Chronic Disease…

Based on our probability adjusted DCF model that takes into account potential future revenues of IMC-1, VIRI is valued at $22.00/share. This model is highly dependent upon continued clinical success of IMC-1 and will be adjusted accordingly based on future clinical results.

Current Price (05/18/21)	$4.75
Valuation	**$22.00**

OUTLOOK

We are initiating coverage of Virios Therapeutics, Inc. (VIRI) with a $22.00 valuation. Virios' lead development candidate is IMC-1, a combination therapy of famciclovir and celecoxib that is designed to treat chronic diseases that are thought to be caused by a heightened immune response to an active herpes simplex virus-1 (HSV-1) infection. The lead indication is fibromyalgia, for which current treatment options are lacking both in terms of efficacy and side effect profile, with plans to expand to irritable bowel syndrome (IBS) and chronic fatigue syndrome (CFS). Virios will be initiating a Phase 2b clinical trial of IMC-1 in FM patients in the second quarter of 2021, with topline results expected in the second quarter of 2022.

SUMMARY DATA

52-Week High	**$16.71**
52-Week Low	**$4.71**
One-Year Return (%)	**N/A**
Beta	**N/A**
Average Daily Volume (sh)	**27,948**
Shares Outstanding (mil)	**8**
Market Capitalization ($mil)	**$40**
Short Interest Ratio (days)	**N/A**
Institutional Ownership (%)	**7**
Insider Ownership (%)	**N/A**
Annual Cash Dividend	**$0.00**
Dividend Yield (%)	**0.00**
5-Yr. Historical Growth Rates	
Sales (%)	**N/A**
Earnings Per Share (%)	**N/A**
Dividend (%)	**N/A**
P/E using TTM EPS	**N/A**
P/E using 2021 Estimate	**N/A**
P/E using 2022 Estimate	**N/A**

Risk Level	**N/A**
Type of Stock	**N/A**
Industry	**Med-Biomed/Gene**

ZACKS ESTIMATES

Revenue
(In millions of $)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2020	0 A	0 A	0 A	0 A	0 A
2021	0 A	0 E	0 E	0 E	0 E
2022					0 E
2023					0 E

Earnings per Share

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2020				-$1.25 A	-$2.10 A
2021	-$0.37 A	-$0.57 E	-$0.70 E	-$0.83 E	-$2.46 E
2022					-$3.05 E
2023					-$2.73 E

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WHAT'S NEW

Initiating Coverage

We are initiating coverage of Virios Therapeutics, Inc. (VIRI) with a valuation of $22.00. Virios is a biopharmaceutical company developing novel therapies for diseases that are triggered by an abnormal immune response to chronic viral infection. The company's lead candidate, IMC-1, is a combination therapy of famciclovir and celecoxib, which is designed to inhibit the activation of tissue resident herpes simplex virus-1 (HSV-1), which has been hypothesized as a potential catalyst in multiple chronic illnesses such as fibromyalgia (FM), irritable bowel syndrome (IBS), and chronic fatigue syndrome (CFS). This is the only anti-viral medicine under development that we are aware of for the treatment of the aforementioned chronic conditions, and this novel approach to treating these ailments could lead to a breakthrough in an area of great unmet medical need. In fact, IMC-1 has been granted Fast Track review designation by the U.S. FDA, which we believe to be the first such designation for a FM development candidate.

Targeting the Source of Chronic Illnesses
Little is known about the root cause of various chronic illnesses such as FM, although research on the role of HSV-1 may help explain how and why these patients get sick. A tissue biopsy study showed that patients with FM and gastrointestinal complaints were much more likely to test positive for activated, replicating HSV-1 infection compared to set of healthy controls. IMC-1 is designed to suppress HSV-1, thereby alleviating the chronic immune response that may be contributing to the aberrant central pain processing found in FM patients.

Current Treatments for FM Are Inadequate
Patients with FM are at an increased risk of mortality due to suicide or accident. This may be due to current treatment options that do not adequately manage the symptoms of the disease. Lyrica® (pregabalin), Cymbalta® (duloxetine), and Savella® (milnacipran) are all FDA approved for the treatment of FM, however each is associated with a number of serious side effects and many patients report a lack of efficacy that typically leads to discontinuation of treatment within a year.

Fibromyalgia Market Large with Room for Growth
Of the estimated 10 million patients in the U.S. with FM, only approximately 20% are currently being treated. In addition, treated patients are typically on multiple therapies at the same time. Lyrica had estimated sales of >$1 billion in 2018 for FM before losing patent protection in 2019. With only 15% of FM treatment prescribers being satisfied with currently available therapies, there is ample opportunity for more effective treatments to gain market share.

Encouraging Proof-of-Concept Results
Virios previously conducted a Phase 2a clinical trial of IMC-1 in 143 FM patients. The randomized, double blind, placebo controlled study showed that treatment with IMC-1 resulted in a statistically significant improvement in chronic pain when measured by two different metrics. Furthermore, IMC-1 treated patients demonstrated statistically significant reductions in FM related fatigue, depression, and anxiety, as well as statistically significant improvements in patient functionality, sleep, and overall quality of health. In addition, IMC-1 treated patients required significantly less opioid pain rescue therapy as compared with placebo treated patients, representing an important finding given the present focus on reducing overall opioid use for patients across the globe. And finally, the drug was very well tolerated as a higher percentage of placebo-treated patients discontinued treatment due to adverse events than IMC-1-treated patients.

Phase 2b Results in 2Q22
A Phase 2b trial of IMC-1 in FM patients is expected to initiate in the second quarter of 2021. Approximately 460 patients will be randomized 1:1 to receive either IMC-1 or placebo and we anticipate topline results in the second quarter of 2022.

INVESTMENT THESIS

Virios Therapeutics, Inc. (VIRI) is a biopharmaceutical company developing therapies for the treatment of chronic illnesses that stem from a viral-induced immune response. The company's lead development product, IMC-1, is a combination therapy designed to suppress the activation of latent, tissue resident Herpes Simplex Virus-1 (HSV-1), which has been proposed as a root cause of chronic illness such as fibromyalgia (FM), irritable bowel syndrome (IBS), and chronic fatigue syndrome (CFS). IMC-1 contains a fixed-dose combination of famciclovir (to inhibit viral DNA synthesis) and celecoxib (which inhibits COX-2, an enzyme necessary for maximal viral replication). Virios will be initiating a Phase 2b clinical trial in FM in the second quarter of 2021 and we anticipate topline results in the second quarter of 2022. While the focus is currently on FM, Virios may investigate IMC-1 as a treatment for IBS and CFS in the future.

Fibromyalgia

Fibromyalgia (FM) is a relatively common condition that is characterized by chronic, widespread pain that occurs for ≥ 3 months along with other systemic symptoms such as sleep disturbance, anxiety, fatigue, and depression (Wang *et al*., 2015). Depending on the methodology, FM is estimated to affect approximately 1-8% of the population (Chinn *et al*., 2016), with females affected at an approximately 3:1 ratio compared to males. FM patients exact a high burden on the healthcare system, with the average FM patient making 10 outpatient medical visits per year, putting it on par to patients with diabetes and hypertension (Wolfe *et al*., 1997). As the following figure on the left shows, an estimated 10 million Americans suffer from FM, however only 36% are diagnosed and 20% receive treatment. In addition, with a worldwide prevalence of 3-6%, there are an estimated 221 million to 447 million FM patients around the world.



Source: Virios Therapeutics, Inc.

Diagnosing FM continues to be somewhat difficult, however recent advances in diagnostic tests are helping to differentiate FM from other disorders. The first attempt at FM classification criteria was in 1990 and was based on studies performed across the U.S. and Canada (Wolfe *et al*., 1990). Since then, there have been multiple revisions to the diagnostic criteria, including a 2016 revision (Wolfe *et al*., 2016) and in 2019, a classification in the International Classification of Diseases (ICD-11) where FM was classified as chronic primary pain to distinguish it from pain secondary to another disease (Treede *et al*., 2019). Recent advances in immunophenotyping have revealed a role for the Mu opioid receptor on B lymphocytes as a specific biomarker for FM (Raffaeli *et al*., 2020) and another biomarker using vibrational spectroscopy was able to different FM patients from those with other pain-related diseases (Hackshaw *et al*., 2019). These tests may aid physicians in diagnosing the condition more easily as well as contribute to legitimizing FM as a unique, painful disease.

FM Treatments

The treatment of FM currently centers on maintaining or improving the patient's quality of life, their ability to function, and managing symptoms of the disease. Initially, FM therapy should focus on educating the patient about the disease and the self-management strategies available to them. Stress management, getting more high-quality sleep, eating healthy, regular physical activity, and maintaining a healthy weight are all nonpharmacologic therapy approaches that form the foundation of FM treatment (Macfarlane *et al*., 2017).

Following initiation of nonpharmacologic treatments, there are currently several classes of medications that are used to control FM symptoms, although each of them has several shortcomings regarding efficacy and possible side effects. There are only three FDA approved drugs to treat FM: Lyrica (pregabalin), Cymbalta (duloxetine), and Savella (milnacipran). Lyrica and Cymbalta have both gone off-patent and Savella will lose patent protection in Jan 2023.

Lyrica (pregabalin): Pregabalin was approved by the FDA for the treatment of FM in 2007. It is a gamma-aminobutyric acid (GABA) analog and α-2-Δ subunit receptor ligand, which ultimately leads to a reduction in the release of several neurotransmitters and reduces the hyper-excitability in the pain processing pathway (Cunningham *et al*., 2004). A randomized, double blind, placebo controlled Phase 3 clinical trial of pregabalin showed a statistically significant reduction of endpoint mean pain scores for all treatment groups (300, 450, and 600 mg) compared to placebo (Arnold *et al*., 2008). The Phase 3 FREEDOM trial enriched for responders before evaluating the durability of response in pregabalin-treated patients compared to placebo-treated patients. Results of that study showed the time to loss of therapeutic response was significantly longer for the pregabalin group compared to the placebo group (Crofford *et al*., 2008). A meta-analysis of clinical trials of pregabalin showed that responses were greatest at 450 mg/day but only approximately one-third of total patients were able to achieve the clinically meaningful benefit in pain response of >30% reduction of pain (Moore *et a*l., 2009).

Side effects from pregabalin therapy are common, with the most frequently reported side effect being dizziness and somnolence, which occur in approximately 40-50% and 30-45% of patients, respectively. Additional common side effects are weight gain and peripheral edema, which are more likely to result in a discontinuation of therapy. Less common side effects include blurred vision and cognitive problems (thinking abnormally, confusion, impaired attention).

In 2018, its last full year of patent protection, sales of Lyrica totaled $5 billion, with approximately $1.1 billion of that for FM (EvaluatePharma).

Cymbalta (duloxetine): Duloxetine was approved by the FDA for the treatment of FM in 2008. It is a selective serotonin and norepinephrine reuptake inhibitor (SNRI). The analgesic effect of duloxetine may be due to its blockade of the sodium ion channel (Wang *et al*., 2010). A randomized, double blind, placebo controlled Phase 3 trial of 354 females showed a statistically significant improvement in mean pain scores from baseline for duloxetine treated patients (both 60 mg and 120 mg daily) compared to placebo-treated patients following 12 weeks of treatment (Arnold *et al*., 2005). A six-month randomized, double blind, placebo controlled trial compared once daily duloxetine (20 mg, 60 mg, or 120 mg/day) to placebo, with the 20 mg/day group titrating to 60 mg/day after three months. Treatment with 120 mg/day duloxetine significantly improved both co-primary outcome measures (Brief Pain Inventory average pain severity score and Patient Global Impressions of Improvement) while the 60 mg/day group showed a significant improvement in both measures at three months and for the Brief Pain Inventory at six months (Russell *et al*., 2008). A Cochrane review concluded that duloxetine had a clinically relevant benefit compared to placebo for pain relief >30% but no clinically relevant benefit over placebo for pain relief of >50% (Welsch *et al*., 2018).

Common side effects reported for duloxetine include nausea, insomnia, dizziness, constipation, and dry mouth, with one study reporting 21% of patients discontinuing treatment due to an adverse event (Chappell *et al*., 2009). In addition, abrupt discontinuation of SNRI's can result in the development of adverse events, thus patients are typically instructed to gradually taper dosing rather than stopping at all once. Lastly, duloxetine (like all antidepressants) carries a 'black-box warning' for an increased risk of suicide in those less than 25 years of age.

Before losing patent protection in December 2013, sales of Cymbalta generated $5.2 billion in revenue in 2013 (EvaluatePharma).

Savella (milnacipran): Milnacipran was approved by the FDA for the treatment of FM in 2009. It is a SNRI like duloxetine. A randomized, double blind, placebo controlled trial compared milnacipran (100 mg/day or 200 mg/day) to placebo with two composite endpoints: an 'FM responder' satisfied response criteria for improvements in pain, patients global impression of change (PGIC), and physical functioning; an 'FM pain responder' satisfied response criteria for improvements in pain and PGIC. Results showed that a significantly higher percentage of milnacipran-treated patients met criteria as FM responders compared to placebo for both doses (Mease *et al*., 2009). A second randomized, double blind, placebo controlled trial with the same doses and outcome measures found that there was a significantly greater proportion of milnacipran-treated patients who were FM responders at both doses compared to placebo-treated patients (Clauw *et al*., 2008).

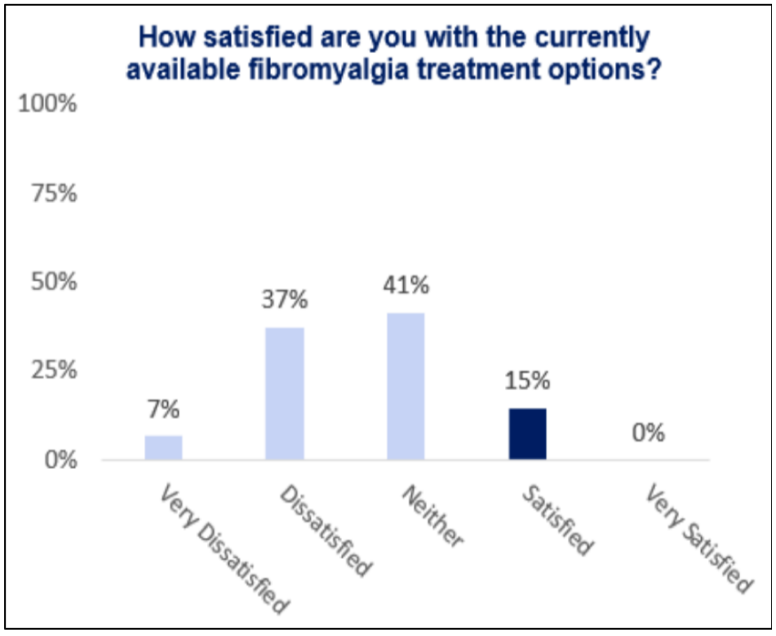
The most commonly reported adverse events for milnacipran-treated patients are nausea, headache, and constipation with approximately 20% of milnacipran-treated patients discontinuing treatment due to adverse events in the above mentioned clinical trials compared to approximately 10% of placebo-treated patients.

Sales of Savella generated revenues of approximately $85 million in 2020, with $55 million of that for FM (EvaluatePharma).

In addition to the above-mentioned FDA approved therapies, additional pharmacotherapies that are routinely prescribed for the treatment of FM include tricyclic antidepressants (amitriptyline, cyclobenzaprine) and opioids. Amitriptyline and cyclobenzaprine have been used to treat FM for decades and a systematic review reported on their effectiveness (O'Malley *et al*., 2000). Opioids have never been shown to be effective in treating FM, however they are still prescribed to a very high percentage of patients (Goldenberg *et al*., 2016), which is of particular concern given the country's ongoing opioid epidemic.

FM Treatments Still Lacking

While there are pharmaceutical treatments available for FM patients, as the following graph shows a large percentage of prescriber's report that they are dissatisfied with current FM treatment options and only 15% report that they are satisfied.



Source: Virios Therapeutics, Inc.

In 2014, the FDA held a public meeting with FM patients to better understand the impact that the disease has on their lives and their experience with currently available therapies (FDA). Patient experiences with prescription drug therapies for FM varied widely, with many participants noting limited benefits or benefits that

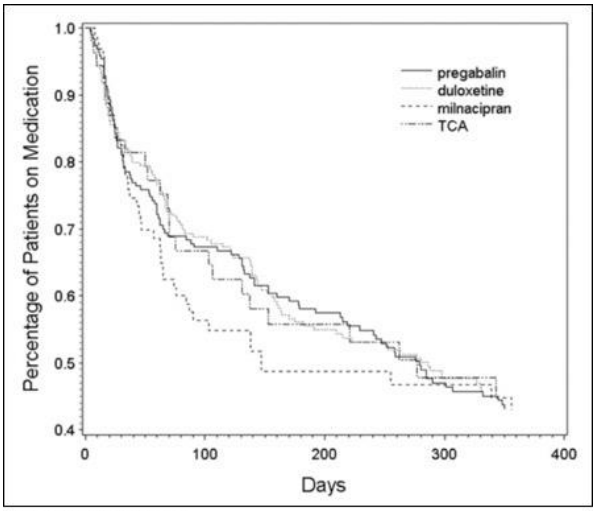
decreased over time. In addition, many participants noted that even if the therapies were effective, they were unable to continue treatment for extended periods of time due to intolerable side effects. Specifically, participants noted the following shortcomings of the FDA approved FM therapies:

- Lyrica – several participants had to discontinue Lyrica after a few weeks due to drowsiness, cognitive issues, dizziness, effects on mood, and weight gain. One participant noted that Lyrica worked for approximately two years, however then it stopped working and had caused a 40-pound weight gain over those two years.

- Cymbalta – several participants noted similar side effects to Lyrica, including significant cognitive issues, weight gain, swelling of the mouth and tongue, vision problems, and suicidal thoughts.

- Savella – many participants noted that Savella was ineffective or had side effects that were intolerable. One participant stated that even though Savella was effective it caused "a year of continual morning sickness" and thus they had to discontinue use.

Lastly, an observational study reported on treatment patterns and outcomes for FM patients over a one-year time period (Robinson *et al*., 2013). Data was collected from 1,700 patients at baseline and at 1, 3, 6, and 12 months. Patients started on 145 different drugs for FM and three-quarters of them took two or more medications concurrently. The following chart shows discontinuation rates for the three FDA approved FM treatments and tricyclic antidepressants (TCA). At 12 months, the estimated discontinuation rates were: pregabalin, 56.9%; duloxetine, 54.2%; milnacipran, 57.1%; and TCA, 54.9%. The most common reason given for discontinuation was adverse events (63.4%) followed by lack of efficacy (30.3%).



Source: Robinson *et al*., 2013

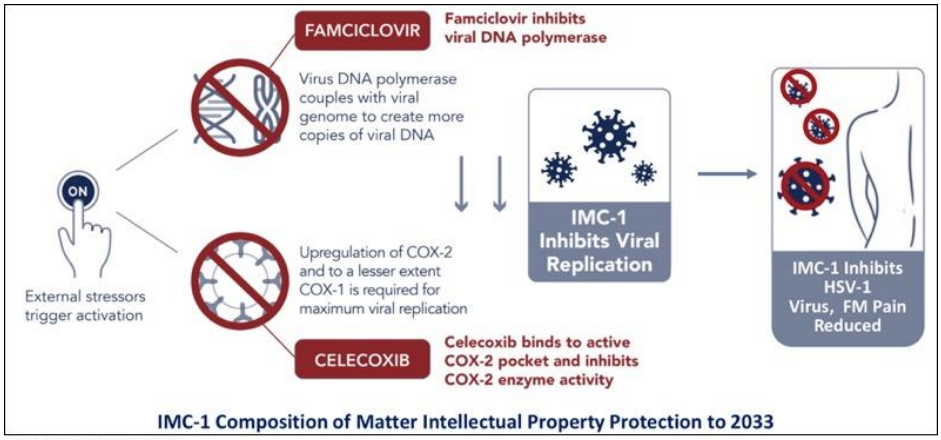
The aforementioned data all point to the fact that there is a pressing need for improved FM therapeutics that are more effective and have better tolerability profiles. In addition, there is a large market opportunity for an additional FM therapeutic, particularly one that is more effective than the currently available treatments. Only approximately 20% (~2 million) of FM patients are diagnosed and on treatment, thus with a full market of 3.6 million diagnosed patients, and a full potential market of 10 million patients, there exists a multi-billion dollar opportunity for a new FM therapy.

New Insights into the Cause of FM

Virios' technology is predicated on the hypothesis that the root cause of FM is an abnormal immune response to a reactivated herpes simplex virus-1 (HSV-1) infection. HSV-1 is a double-stranded DNA virus that causes cold sores in and around the mouth. Approximately 50-80% of adults in the U.S. are infected with the virus, however not everyone shows signs of infection. Once infected, an individual with HSV-1 will have the virus for the rest of their life, with the virus normally residing dormant in neuronal nuclei.

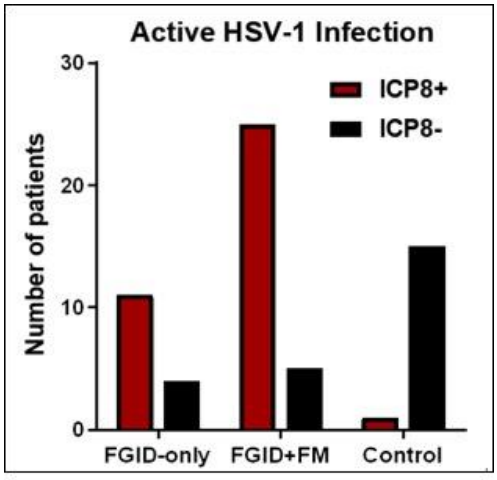
The impetus for using an antiviral plus a COX-2 inhibitor as a treatment for FM was based on the observation that patients with irritable bowel syndrome (IBS) treated with famciclovir, who also happened to be taking celecoxib concurrently to treat other conditions (e.g., osteoarthritis), showed significant improvement in their IBS, FM, fatigue, and headaches. This observation lead to the hypothesis that stress or other environmental factors reactivate a latent HSV-1 infection that results in a continuous nociceptive stimulation and heightened immune response. (Bond, 1993).

IMC-1, Virios' lead development product, consists of a proprietary mixture of the anti-viral drug famciclovir and the COX-2 inhibitor celecoxib. Famciclovir is a guanosine analogue that was first approved by the FDA in 1994 and is used for the treatment of various herpesvirus infections (shingles, cold sores, genital herpes). It works through inhibition of DNA replication. Celecoxib is a nonsteroidal anti-inflammatory drug (NSAID) that is highly selective for the COX-2 isoform of cycolooxygenase and is used to treat pain and inflammation. Non-selective NSAIDs (aspirin, ibuprofen, naproxen) inhibit both COX-1 and COX-2 and are associated with gastrointestinal side effects, which a COX-2 selective inhibitor can minimize. In addition to its analgesic and anti-inflammatory properties, COX-2 inhibitors were shown to suppress HSV-1 activation (Gebhardt *et al*., 2005). Thus, by combining famciclovir and celecoxib, Virios is hoping to return HSV-1 to a dormant state through two separate mechanisms of action and decrease the associated aberrant immune response.



Source: Virios Therapeutics, Inc.

Support for the hypothesis of HSV-1 activation leading to immune dysfunction was shown in a study of gastrointestinal (GI) tissue samples from patients with FM. The study was conducted in partnership with Dr. Carol Duffy at the University of Alabama. Thirty FM patients with chronic GI complaints and 15 control patients submitted biopsy specimens, which were analyzed for HSV-1 infection by immunoblot analysis for the viral non-structural protein ICP8, which is only found during activated, replicating HSV-1 infection, along with PCR to detect herpesvirus DNA. The following figure shows that active HSV-1 infection was found in 83% of FM+GI patients but only 9% of control subjects ($P<0.0001$). The study also examined IBS patients, for which there was a strong correlation with active HSV-1 infection ($P=0.0005$).



Source: Virios Therapeutics, Inc.

Phase 2a Trial Results

Virios (then known as Innovative Med Concepts, LLC) previously conducted the PRID-201 study to evaluate the safety and efficacy of IMC-1 in patients with FM (NCT01850420). This was a 16-week, multicenter, randomized, double blind, placebo controlled Phase 2a proof-of-concept trial in which patients received either IMC-1 or placebo in a 1:1 ratio (Pridgen *et al*., 2017). The primary efficacy outcome measure was a change from baseline in FM pain, which was assessed using the 24-hour recall average pain score recorded using the 11-point Numerical Rating Scale (NRS), as well as the 7-day recall average pain score recorded on the Revised Fibromyalgia Impact Questionnaire (FIQ-R) at baseline and Weeks 6, 12, and 16. In addition, patients completed the Beck Depression Inventory (BDI-II), Multidimensional Fatigue Inventory (MFI), the NIH Patient-Reported Outcomes Measurement Information System (PROMIS) fatigue questionnaire, and the Patient Global Impression of Change (PGIC) at baseline and Weeks 6, 12, and 16.

Results from the trial showed that treatment with IMC-1 lead to a statistically significant improvement in the chronic pain of FM patients as judged by either metric – the 24-hour recall average pain score or the 7-day recall average pain score, as shown in the following figure.

PRID-201 Phase 2a Primary Endpoint Analysis

Pain Analysis	Placebo LS Change @ Endpoint (SE)		IMC-1 LS Change @ Endpoint (SE)		Contrast (SE)		P- Value
NRS 24-hour recall, MMRM LOCF/BOCF Imputation @ 16 weeks	-1.1	(0.28)	-1.9	(0.28)	-0.8	(0.37)	0.031
FIQ-R 7-days recall, MMRM LOCF/BOCF Imputation @ 16 weeks	-0.92	(0.30)	-2.2	(0.30)	-1.25	(0.38)	0.001

Source: Virios Therapeutics, Inc.

An additional pain outcome was the total number of 50% pain responders, which is analyzed by performing a generalized linear regression curve fit to an individual patient's data to determine if the estimated change from baseline for a patient's pain scores were ≥50%. As the following figure shows, there were statistically significantly more 50% pain responders in the IMC-1-treated group than in the placebo-treated group. For the 30% reduction in pain, the 7-day recall was statistically significant but the 24-hour NRS narrowly missed achievement of statistical significance.

PRID-201 Phase 2a Secondary Endpoint 50% Reduction of Pain Analyses with Curve Fit

50% Pain Responder Analysis	Measure	Placebo Responders (%)		Placebo Non-Responders (%)		IMC-1 Responders (%)		IMC-1 Non-Responders		P-Value
Week 16 Visit, 50% Reduction	NRS	11	(15.1)	62	(84.9)	20	(30.3)	46	(69.7)	0.009
Week 16 Visit, 50% Reduction	FIQ-R Pain	12	(16.9)	59	(83.1)	25	(37.9)	41	(62.1)	0.001

PRID-201 Phase 2a Secondary Endpoint 30% Reduction of Pain Analyses with Curve Fit

30% Pain Responder Analysis	Measure	Placebo Responders (%)		Placebo Non-Responders (%)		IMC-1 Responders (%)		IMC-1 Non-Responders		P-Value
Week 16 Visit, 30% Reduction	NRS	23	(31.5)	50	(68.5)	28	(42.4)	38	(57.6)	0.052
Week 16 Visit, 30% Reduction	FIQ-R Pain	20	(28.2)	51	(71.8)	29	(43.9)	37	(56.1)	0.012

Source: Virios Therapeutics, Inc.

The PGIC is a patient's own assessment of how well a therapy is working for them and previous FM studies have shown it to be a sensitive measure of therapeutic benefit in the context of other outcome measurements (Rampakakis *et al*., 2015). It was a pre-specified secondary endpoint and the results are shown below. The PGIC responder analysis was significant at the 6, 12, and 16-week visits.

PRID-201 Phase 2a Secondary Endpoint Patient Global Impression of Change Result

PGIC Analysis	Placebo Responders (%)		Placebo Non-Responders (%)		IMC-1 Responders (%)		IMC-1 Non-Responders		P- Value
Week 6 Visit	14	(19.2)	59	(80.8)	26	(37.7)	43	(62.3)	0.040
Week 12 Visit	13	(17.8)	60	(82.2)	26	(37.7)	43	(62.3)	0.005
Week 16 Visit	14	(19.2)	59	(80.8)	23	(33.3)	46	(66.6)	0.040

Source: Virios Therapeutics, Inc.

The FIQ-R is a widely used and well validated means to assess functional capacity and global impact of FM and associated symptoms. It demonstrated statistical significance in all three domains, as shown below.

Analysis of FIQ-R Domain Scores with LOCF/BOCF Imputation

Week 16 FIQ-R Analysis LOCF/BOCF Imputation)*	LS Mean (SE) Change from Baseline Placebo N = 71		IMC-1 N = 66		Contrast (SE)		P- Value**
Functional Domain	-5.44	(2.32)	-14.29	(2.40)	-8.85	(3.03)	0.004
Overall Impact Domain	-1.89	(0.61)	-4.29	(0.63)	-2.40	(0.79)	0.003
Symptoms Domain	-7.90	(2.33)	-16.77	(2.40)	-8.88	(3.06)	0.004

* LOCF/BOCF imputation = BOCF for missing data due to withdrawals related to adverse events or lack of efficacy or LOCF for missing data unrelated to efficacy or adverse events.

** Obtained from MMRM model with treatment as the main effect, and investigative site and Baseline score as covariates.

Source: Virios Therapeutics, Inc.

The side effect profile for IMC-1 was highly favorable and IMC-1 actually showed greater tolerability than placebo in the PRID-201 trial. The following table shows adverse events that were reported by ≥5% of patients in either treatment group. Interestingly, GI side effects (diarrhea, nausea, vomiting) were reported much more in the placebo group than the IMC-1 group. GI side effects are a known symptom of FM. There were no deaths reported during the study and three serious adverse events (SAEs), two in the IMC-1 group and one in the placebo group. Only one SAE was considered possibly related to study treatment – a non-ST segment elevation myocardial infarction that occurred in a 47-year old patient who had underlying coronary artery disease and a strong family history of premature cardiac disease.

PRID-201 Phase 2a Adverse Event Report

Adverse Events Reported for ≥5% of the Patients in Either Treatment Group

Adverse Event	Placebo N=73		IMC-1 N=69	
Any Event	57	(78.1)%	50	(72.5)%
Headache	10	(13.7)%	8	(11.6)%
Urinary Tract Infection	4	(5.5)%	6	(8.7)%
Blood Lactate Dehydrogenase Increased	1	(1.4)%	4	(5.8)%
Nasopharyngitis	1	(1.4)%	4	(5.8)%
Diarrhea	9	(12.3)%	3	(4.3)%
Nausea	13	(17.8)%	3	(4.3)%
Fibromyalgia	4	(5.5)%	2	(2.9)%
Vomiting	5	(6.8)%	2	(2.9)%

Adverse Events Reported for ≥5% of the Patients in Either Treatment Group

Adverse Event	Placebo N=73		IMC-1 N=69
Constipation	6	(8.2)%	—
Gastroesophageal Reflux Disease	4	(5.5)%	—
Alopecia	4	(5.5)%	—
Oropharyngeal Pain	4	(5.5)%	—

Source: Virios Therapeutics, Inc.

Lastly, an end-of-study questionnaire asked study participants whether they had suffered common FM conditions during the study and, if so, how those symptoms were now relative to baseline. This questionnaire was performed as an exploratory endpoint. The results were reported as the likelihood of improvement versus placebo for patients on IMC-1 (for example, the following shows that patients on IMC-1 with IBS symptoms were 2.8 times more likely to be improved compared to placebo).

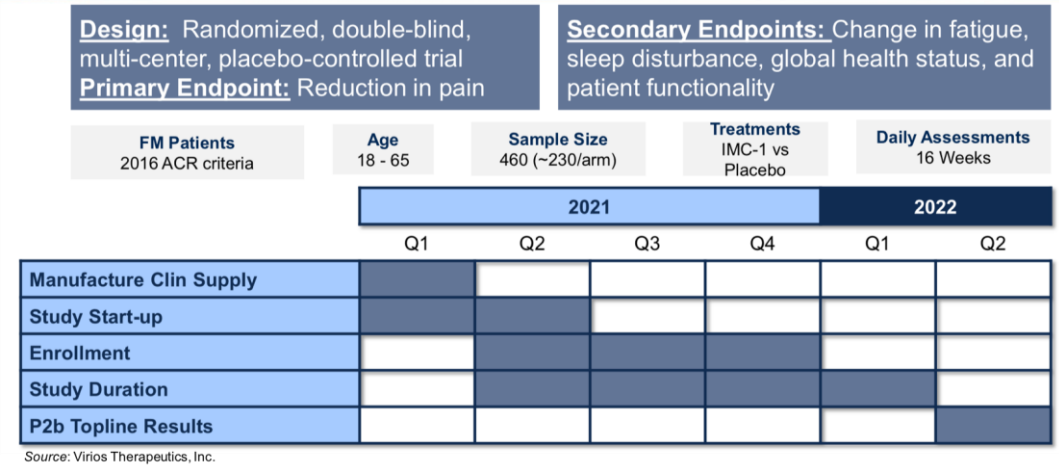
FM and Chronic Fatigue: 2.2 times (improvement vs. placebo)
IBS: 2.8 times
Cognitive Impairment: 2.1 times
Headache: 2.5 times
TMJ: 5 times
Insomnia: 1.7 times
Neck and Back Pain: 2.3 times
Anxiety: 2.8 times
Depression: 1.8 times

Overall, the PRID-201 study successfully provided proof-of-concept results showing improvement for FM patients treated with IMC-1 across a number of different attributes and fully supports IMC-1's continued development as a treatment for FM. In addition, the study was performed with a non-optimized dose of IMC-1, thus these results could be improved upon in later-stage trials with a higher IMC-1 dose.

Phase 2b Trial Design

Following the end of the Phase 2a trial, the company held an 'End-of-Phase 2' meeting with the FDA at which time the agency agreed to a defined path to Phase 3, including the ability to initiate a Phase 2b trial following animal toxicology testing and a human PK study with the dose of IMC-1 that will be used in late-stage trials. The company has finished the human PK study and it did not reveal any unexpected findings. The 90-day and 13-week animal toxicology studies are also complete and there were no unexpected toxicities from IMC-1, with all toxicities shown being consistent with the known toxicities of celecoxib and famciclovir. In order to support long-term dosing with IMC-1, the company will perform a chronic toxicology study that will run in parallel with the Phase 2b trial.

An outline of the Phase 2b study design and timeline are shown below. It will be a randomized, double blind, placebo controlled, multi-center trial with a primary endpoint of reduction in pain and secondary endpoints including change in fatigue, sleep disturbance, global health status, and patient functionality. Approximately 460 females between the ages of 18-65 will be enrolled with a study duration of 16 weeks. We anticipate enrollment initiating in the second quarter of 2021 and topline results are expected in the second quarter of 2022.



Source: Virios Therapeutics, Inc.

Intellectual Property

As of December 31, 2020, Virios had a total of 20 issued patents, including 12 issued U.S. patents and 8 issued foreign patents. Included in that group of patents are three composition of matter patents (including a synergistic patent) and two method of use patents. Exclusivity with all the patents is through 2033.

Issued U.S. IMC-1 Patents:
U.S. 8,809,351 & U.S. 10,034,846 – Drug-combination of famciclovir and celecoxib
U.S. 9,040,546 – Famciclovir+celecoxib for the treatment of FM, CFS, or IBS
U.S. 9,173,863 – Method of dispensing famciclovir+celecoxib to treat Functional Somatic Syndrome conditions
U.S. 10,251,853 – Synergistic combination of famciclovir+celecoxib for daily use

Issued Foreign IMC-1 Patents:
European (EP 2 811 833 & 2 965 759)
Japan (JP 5855770 & 6422848)
Australia (AU 2013217110)
China (CN 104144606)
Korea (KR 10-1485748)
Canada (2,863,812)

In addition to the above patents for IMC-1, the company has a number of patents covering other anti-viral combinations:

U.S. 9,682,051 (acyclovir/meloxicam)
U.S. 8,623,882 (acyclovir/diclofenac)
U.S. 9,259,405 (famciclovir/diclofenac)
U.S. 9,642,824 (valacyclovir/diclofenac)
U.S. 9,980,932 (valacyclovir/meloxicam)
U.S. 10,543,184 (acyclovir/celecoxib)
U.S. 10,632,087 (famciclovir/meloxicam)
EP 2 965 759

Financials and Capital Structure

On May 13, 2021, Virios announced financial results for the first quarter of 2021. As expected, the company did not report any revenues for the first quarter of 2021. R&D expenses for the three months ending March 31, 2021 were $1.71million, compared to $0.03 million for three months ending March 31, 2020. The increase was primarily due to increased expenses for clinical trials, toxicology studies, salaries, and drug development and manufacturing. G&A expenses were $1.35 million for the first quarter of 2021, compared to $0.35 million for the first quarter of 2020. The increase was primarily due to increased salaries, legal fees, and other costs associated with being a public company.

As of March 31, 2021, Virios had approximately $24.6 million in cash and cash equivalents due in part to the company's initial public offering on December 20, 2020 that raised net proceeds of approximately $31.1 million. We estimate the company has sufficient capital to fund operations through the end of 2022. As of May 13, 2021, Virios had approximately 8.3 million common shares outstanding and, when factoring in stock options and warrants, a fully diluted share count of approximately 9.3 million.

Risks to Consider

Clinical Risk: While the results from the Phase 2a clinical trial of IMC-1 were positive, there is no guarantee that those results will be replicated in a Phase 2b or Phase 3 trial with a larger number of patients. In addition, while there were no safety concerns or tolerability issues in the Phase 2a trial, the Phase 2b trial will be testing a different dose of IMC-1 that could result in a different adverse event profile.

Development Risk: IMC-1 is Virios' only product under development, thus failure to advance it through clinical trials and to approval would be highly negative for the company. There are already three approved treatments for fibromyalgia, thus even if IMC-1 is approved there is no guarantee it will be accepted by physicians, payers, and/or patients. Other companies may develop products that could exhibit better effectiveness or increased safety as compared with IMC-1. While the company is planning to develop IMC-1 as a treatment for other conditions such as IBS and CFS, there is no guarantee that it will be successful in those areas.

Financing Risk: Virios is not currently profitable and will require substantial additional capital in order to advance IMC-1 through clinical testing and to approval. As of December 31, 2020, the company had approximately $29.8 million in cash and cash equivalents, which we estimate is sufficient to fund operations through 2022, including the Phase 2b trial. However, the company will need additional cash to conduct a Phase 3 program for IMC-1.

Stock Risk: Virios' initial public offering was on December 21, 2020 and even though the stock is traded on the Nasdaq thus far it has very limited liquidity. Thus, the share price could be subject to large daily fluctuations.

MANAGEMENT PROFILES

Greg Duncan – Chief Executive Officer and Chairman of the Board of Directors

Mr. Duncan is the Chief Executive Officer and Chairman of the Board of Directors of Virios Therapeutics. Previously, Mr. Duncan was President and Chief Executive Officer of Celtaxsys, Inc., a privately held biotech company focused on developing anti-inflammatory medicines for rare disease where he scaled the required capital to build out the organizational capability to advance both pre- clinical and clinical development candidates. Prior to Celtaxsys, he served as an Executive Committee member at Belgium based UCB, a specialty pharma entity developing and commercializing medicines for immunologic and central nervous system disorders. Before joining UCB, Mr. Duncan held several executive U.S. and international appointments at Pfizer over his 17-year tenure, including President of Pfizer's $2B Latin America Operations and SVP of US Marketing. His operational teams had accountability for the launches of many pharmaceutical brands including Lipitor, Zoloft, Viagra, Celebrex, Aricept, Lyrica, Cimzia, Zithromax (ZPack), Diflucan, Sutent, Rebif and Vimpat. Mr. Duncan serves as an independent director at Cormedix, Inc (ticker: "CRMD") and has served as director for Biotie Therapeutics, the American Psychiatric Foundation, Bio International Organization (BIO), Southeast BIO (SEBIO) and the Georgia Bio industry association groups. Greg holds a master's degree in business administration from Emory University in Atlanta, GA, and a bachelor's degree in economics from the State University of New York in Albany, NY.

R. Michael Gendreau, MD, PhD – Chief Medical Officer

Dr. Gendreau is the Chief Medical Officer of Virios Therapeutics. Dr. Gendreau has been a healthcare consultant specializing in biotechnology for Gendreau Consulting, LLC. He received his B.S. in chemistry from Ohio University and his M.D./Ph.D. in medicine and pharmacology from The Ohio State University College of Medicine. Before starting his own consulting firm, Dr. Gendreau worked at Cypress Bioscience, Inc. holding various positions including Vice President of Research and Development and Chief Medical Officer. Before joining Cypress Bioscience, Inc., Dr. Gendreau was Vice President of Research and Development and Chief Medical Officer for MicroProbe Corporation, a developer and manufacturer of DNA/RNA probe-based diagnostic products.

Ralph Grosswald – Vice President of Operations

Mr. Grosswald has 25 years of experience developing innovative drugs and medical devices. Previously, Mr. Grosswald was a founder and Vice President of Operations at Celtaxsys, Inc. where he managed operations, nonclinical development and clinical trials of acebilustat for the treatment of cystic fibrosis. Prior to that, Mr. Grosswald started GMP Companies, Inc. where he managed the programs of the first ever Microinvasive Glaucoma Shunt and the LifeSync Wireless ECG. Before joining GMP, he was the Director of Outcomes Research for the National Healthcare Network, a cardiovascular centers of excellence managed care network partnered with the Duke Clinical Research Institute. Mr. Grosswald began his career as a clinical trial coordinator for both interventional cardiology and cardiothoracic surgery studies at the Emory University School of Medicine from 1990 to 1997. Mr. Grosswald holds B.A. and Master of Public Health degrees from Emory University.

Angela Walsh – Senior Vice President of Finance & Treasurer

Ms. Walsh is the Senior Vice President of Finance and Treasurer of Virios Therapeutics. Ms. Walsh has over three decades of experience in the field of financial management and accounting, specializing in mergers and acquisitions, strategic planning, compliance and risk management, financial modeling, budgeting, and forecasting. She was the VP of Finance for Celtaxsys, Inc. where she oversaw and managed the company's financial and accounting activities. Prior to that, Ms. Walsh worked at Vennskap, LLC and was the CFO for Green Circle Bio Energy where she part of the executive team that executed a successful acquisition by Enviva Partners, LP, which subsequently executed a $214M initial public offering. Prior to that, she worked at Atlanco and at Altea Therapeutics. Ms. Walsh was the Controller for Huffy Sports, a division of the Russell Corporation and participated in numerous capital market transactions including mergers and acquisitions, debt offerings and filing S-1s for initial public offerings. Ms. Walsh began her accounting career with Arthur Anderson and is a Certified Public Accountant in both Georgia and North Carolina. Ms. Walsh holds a BS in Accounting from Wake Forest University.

VALUATION

We are initiating coverage of Virios Therapeutics, Inc. (VIRI) with a valuation of $22.00. Virios is a biopharmaceutical company developing novel therapies for diseases that are triggered by an abnormal immune response to chronic viral infection. The company's lead candidate, IMC-1, is a combination therapy of famciclovir and celecoxib, which is designed to inhibit the activation of tissue resident herpes simplex virus-1 (HSV-1), which has been hypothesized as a potential catalyst in multiple chronic illnesses such as fibromyalgia (FM), irritable bowel syndrome (IBS), and chronic fatigue syndrome (CFS). This is the only anti-viral medicine under development that we are aware of for the treatment of the aforementioned chronic conditions, and this novel approach to treating these ailments could lead to a breakthrough in an area of great unmet medical need. In fact, IMC-1 has been granted Fast Track review designation by the U.S. FDA, which we believe to be the first such designation for a FM development candidate.

IMC-1

IMC-1 consists of a proprietary mixture of the anti-viral drug famciclovir and the COX-2 inhibitor celecoxib. Famciclovir is a guanosine analogue that was first approved by the FDA in 1994 and is used for the treatment of various herpesvirus infections (shingles, cold sores, genital herpes). It works through inhibition of DNA replication. Celecoxib is a nonsteroidal anti-inflammatory drug (NSAID) that is highly selective for the COX-2 isoform of cycloooxygenase and is used to treat pain and inflammation.

Support for the hypothesis of HSV-1 activation leading to immune dysfunction was shown in a study of gastrointestinal (GI) tissue samples from patients with FM. The study was conducted in partnership with Dr. Carol Duffy at the University of Alabama. Thirty FM patients with chronic GI complaints and 15 control patients submitted biopsy specimens, which were analyzed for HSV-1 infection by immunoblot analysis for the viral non-structural protein ICP8, which is only found during activated, replicating HSV-1 infection, along with PCR to detect herpesvirus DNA. Active HSV-1 infection was found in 83% of FM+GI patients but only 9% of control subjects ($P<0.0001$). The study also examined IBS patients, for which there was a strong correlation with active HSV-1 infection ($P=0.0005$).

Virios previously conducted the PRID-201 study to evaluate the safety and efficacy of IMC-1 in patients with FM. It was a 16-week, multicenter, randomized, double blind, placebo controlled Phase 2a proof-of-concept trial in which patients received either IMC-1 or placebo in a 1:1 ratio. Results from the trial showed that treatment with IMC-1 lead to a statistically significant improvement in the chronic pain of FM patients as judged by the co-primary outcome metrics – the 24-hour recall average pain score and the 7-day recall average pain score. In addition, multiple secondary outcomes statistically significantly favored IMC-1 and the side effect profile for IMC-1 was highly favorable, with IMC-1 actually showing greater tolerability than placebo.

To follow up on the results of the PRID-201 trial, Virios is planning to initiate a randomized, double blind, placebo controlled, multi-center Phase 2b trial for IMC-1 with a primary endpoint of reduction in pain and secondary endpoints including change in fatigue, sleep disturbance, global health status, and patient functionality. We anticipate the trial getting underway in the second quarter of 2021 and topline results being available in the second quarter of 2022.

Valuation

We value Virios using a probability adjusted discounted cash flow model that takes into account potential future revenues of IMC-1 in FM, while also recognizing the potential value of IMC-1's potential use in other chronic conditions. We model for Virios to partner IMC-1 and to receive a 15% royalty on net sales.

As previously mentioned, we estimate topline results from the upcoming Phase 2b trial of IMC-1 in FM being released in the second quarter of 2022. We model for a Phase 3 program to initiate in 2023, an NDA filing to occur in 2025, and the drug to be approved for FM in 2026. We estimate of the approximately 10 million individuals living with FM, approximately 35% are diagnosed and only 20% are currently on treatment,

however an effective therapeutic would likely increase the percentage of patients on therapy. We model for peak revenues of $1.3 billion, which is in line with the peak revenues for Lyrica in FM before it lost patent exclusivity. Using a 15% royalty rate, a 60% probability of approval, and a 13% discount rate leads to a net present value for IMC-1 in FM of approximately $146 million.

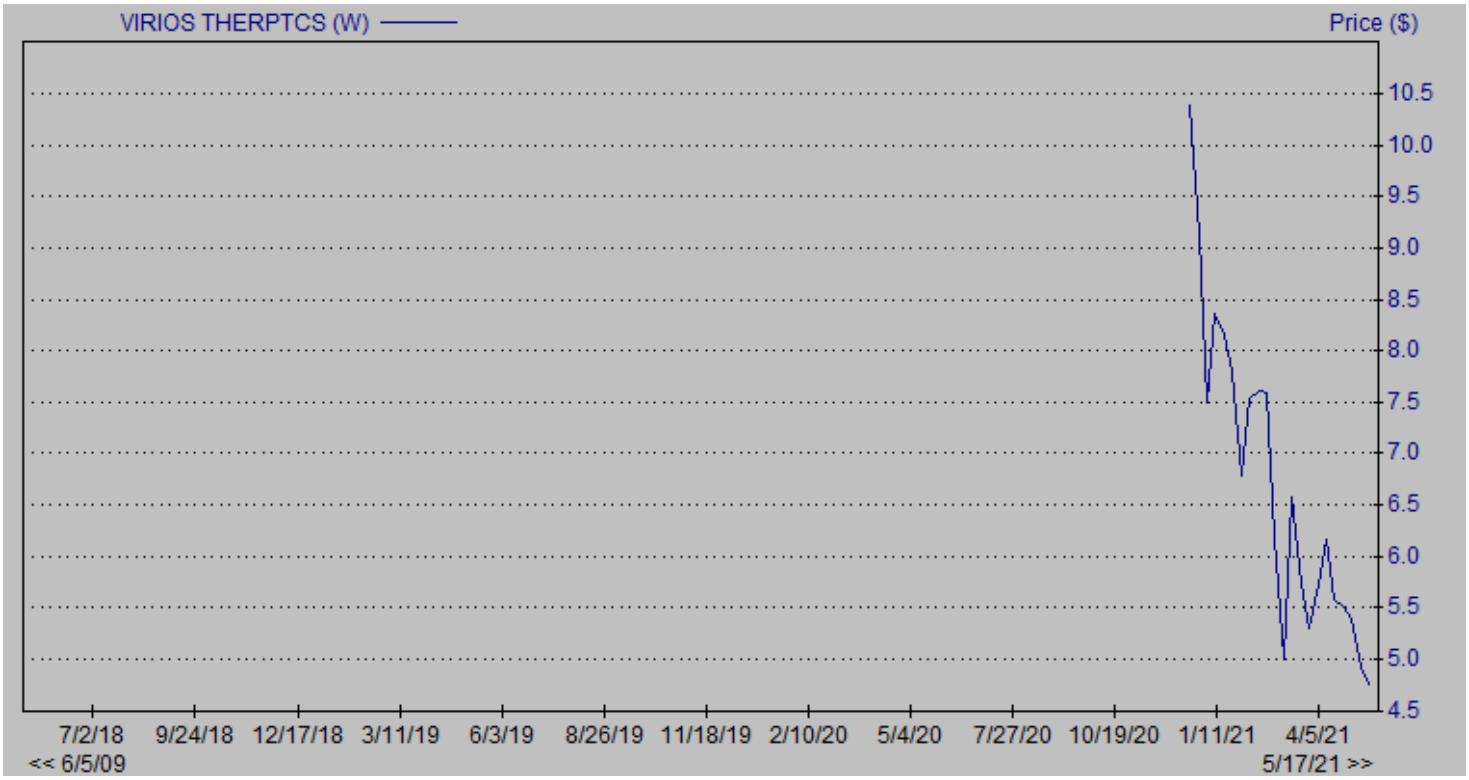
In addition to FM, we assign a value of $100 million for the potential use of IMC-1 in other chronic conditions such as IBS and CFS. Combining the valuation for IMC-1 in FM, other chronic conditions, and the current cash balance leads to a net present value for the company of $271 million. The company's current fully diluted share count is approximately 9.3 million, and we add an additional 3.0 million shares for future financings, which leads to a valuation of $22.00 per share.

PROJECTED FINANCIALS

Virios Therapeutics, Inc.	2020 A	Q1 A	Q2 E	Q3 E	Q4 E	2021 E	2022 E	2023 E
IMC-1	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Other Income	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Total Revenues	**$0.0**	**$0.0**	**$0.0**	**$0.0**	**$0.0**	**$0.0**	**$0.0**	**$0.0**
CoGS	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Product Gross Margin	-	-	-	-	-	-	-	-
R&D	$0.2	$1.7	$2.0	$3.0	$4.0	$10.7	$15.0	$20.0
SG&A	$9.8	$1.4	$2.8	$2.9	$3.0	$10.1	$12.0	$13.0
Operating Income	($10.0)	($3.1)	($4.8)	($5.9)	($7.0)	($20.8)	($27.0)	($33.0)
Operating Margin	-	-	-	-	-	-	-	-
Interest & Other Income	($0.3)	$0.0	$0.0	$0.0	$0.0	$0.1	$0.2	$0.2
Pre-Tax Income	($10.3)	($3.1)	($4.8)	($5.9)	($7.0)	($20.6)	($26.8)	($32.8)
Taxes & Other	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Tax Rate	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*
Net Income	($10.3)	($3.1)	($4.8)	($5.9)	($7.0)	($20.6)	($26.8)	($32.8)
Reported EPS	**($2.10)**	**($0.37)**	**($0.57)**	**($0.70)**	**($0.83)**	**($2.46)**	**($3.05)**	**($2.73)**
Weighted Shares Outstanding	4.9	8.3	8.4	8.4	8.4	8.4	8.8	12.0

Source: Zacks Investment Research, Inc. *David Bautz, PhD*

HISTORICAL STOCK PRICE



Source: Zacks Small Cap Research

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