Zacks Small-Cap Research

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Qualigen Therapeutics, Inc.

(QLGN-NASDAQ)

QLGN: Initiating Coverage of Qualigen Therapeutics, Inc.; Targeting Cancer and Infectious Diseases…

Based on our probability adjusted DCF model that takes into account potential future revenues from ALAN, AS1411, and RAS-F, QLGN is valued at $10.00 per share. This model is highly dependent upon continued clinical success of the company's assets and will be adjusted accordingly based upon future clinical results and the company's execution.

Current Price (09/21/20)	$4.72
Valuation	**$10.00**

OUTLOOK

We are initiating coverage of Qualigen Therapeutics, Inc. (QLGN) with a $10.00 valuation. Qualigen is developing therapeutics for the treatment of cancer and infectious diseases. The pipeline includes ALAN, composed of a DNA aptamer (AS1411) linked to a gold nanoparticle, RAS-F, a family of small molecule RAS protein-protein interaction inhibitors, and STARS™, a treatment device product designed to remove various compounds from circulating blood. The company is also developing AS1411 as a potential treatment for COVID19, with a clinical trial set to initiate in the first half of 2021.

SUMMARY DATA

52-Week High	**$18.05**
52-Week Low	**$3.88**
One-Year Return (%)	**-33.99**
Beta	**-0.43**
Average Daily Volume (sh)	**848,566**
Shares Outstanding (mil)	**21**
Market Capitalization ($mil)	**$99**
Short Interest Ratio (days)	**N/A**
Institutional Ownership (%)	**1**
Insider Ownership (%)	**15**
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 2020 Estimate	**-0.1**
P/E using 2021 Estimate	**-0.3**

Risk Level	**High**
Type of Stock	**Small-Value**
Industry	**Med-Drugs**

ZACKS ESTIMATES

Revenue
(in millions of $)

	Q1 (Jun)	Q2 (Sep)	Q3 (Dec)	Q4 (Mar)	Year (Mar)
2020	1.5 A	1.2 A	1.4 A	1.5 A	5.6 A
2021	0.9 A	1.4 E	1.4 E	1.4 E	5.6 E
2022					5.6 E
2023					5.6 E

Earnings Per Share

	Q1 (Jun)	Q2 (Sep)	Q3 (Dec)	Q4 (Mar)	Year (Mar)
2020	-$0.11 A	-$0.06 A	$0.01 A	-$0.16 A	-$0.32 A
2021	-$2.12 A	-$0.10 E	$0.20 E	$0.26 E	-$0.61 E
2022					-$0.63 E
2023					-$0.69 E

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WHAT'S NEW

Initiating Coverage

We are initiating coverage of Qualigen Therapeutics, Inc. (QLGN) with a valuation of $10.00. Qualigen is a biopharmaceutical company developing novel treatments for cancer and infectious diseases while continuing and expanding its FDA approved FastPack® System. The company's development pipeline includes ALAN, featuring a DNA aptamer (AS1411) linked to a gold nanoparticle, RAS-F, a family of small molecule RAS protein-protein interaction inhibitors, and STARS™, a treatment device product designed to remove various compounds from circulating blood. AS1411 is also being developed as a potential treatment for SARS-CoV-2 infection. The company also markets the FDA approved FastPack System, which includes diagnostic instruments and test kits. Qualigen recently began shipment of a SARS-CoV-2 IgG diagnostic test for COVID antibodies. The FastPack product line is sold worldwide by its commercial partner Sekisui Diagnostics, LLC.

DNA Aptamer Technology
DNA aptamers are short, single stranded oligonucleotides that can selectively bind to a specific target through its three-dimensional shape, much like an antibody. Aptamers have been designed to bind to proteins, peptides, carbohydrates, toxins, and cells. The company's lead aptamer, AS1411, has shown activity in Phase 1 and 2 clinical trials, including a 20% complete remission rate in patients with acute myeloid leukemia (AML).

Next-Generation Aptamer Technology
ALAN (Aptatmer-Linked Anti-Nucleolin) is a next-generation aptamer technology that features an aptamer-coated gold nanoparticle. Gold nanoparticles have a number of positive attributes that make them good drug delivery vectors, including a tunable size, a small size that allows them to pass through capillaries efficiently, and for cancer drug deliver they can collect in tumor tissue due to their leaky vasculature. Preclinical data shows that ALAN inhibits the growth of tumors in a xenograft model of breast cancer.

AS1411 to Treat SARS-CoV-2 Infection
In addition to its anti-cancer activity, AS1411 has shown anti-viral activity in preclinical studies. This will be further evaluated as a treatment for the ongoing coronavirus pandemic, but could also be applicable to other RNA viruses such as influenza, West Nile virus, and Ebola virus.

Targeting RAS Oncogene
RAS proteins are involved in a number of signaling pathways required for cell cycle entry and progression, and mutations in RAS proteins are found in approximately 1/3rd of cancers. Qualigen has identified a group of protein-protein inhibitor compounds that block mutant RAS signaling and inhibit tumor growth in *in vivo* models, with work beginning on selecting a lead development compound.

Funded Through the End of Calendar 2021
The company recently completed two registered direct offerings for gross proceeds of $18 million and the company now has sufficient financing to fund operations through the end of calendar 2021.

INVESTMENT THESIS

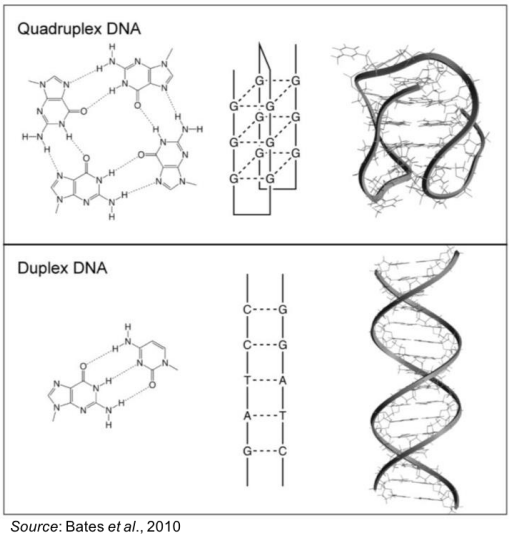
Qualigen Therapeutics, Inc. (QLGN) is a biopharmaceutical company focused on the development of novel treatments for cancer and infectious diseases. The company also markets the FDA approved FastPack® System, which includes diagnostic instruments and test kits. The FastPack product line is sold worldwide by its commercial partner Sekisui Diagnostics, LLC. The development pipeline consists of four lead products: ALAN, which is being developed for the treatment of acute myeloid leukemia, AS1411, which is being developed as a treatment for SARS-CoV-2 infection, RAS-F, a family of small molecule protein-protein interaction inhibitors that target the RAS oncogene, and STARS™, a treatment device designed to remove various components from circulating blood. The company has signed multiple exclusive license agreements with the University of Louisville for the development of AS1411 and RAS-F.



Source: Qualigen Therapeutics, Inc.

DNA Aptamers

The advent of automated DNA synthesizers in the 1980's, which dramatically decreased the cost of producing oligonucleotides, increased the interest in developing DNA and RNA based therapeutics. While most work involving oligonucleotide therapeutics has focused on inhibiting the expression of specific cellular or viral genes (through sequence specific hybridization or RNA interference), early on it was recognized that oligonucleotides that contained a high percentage of guanine (G) bases exhibited unusual properties unrelated to complementary binding and most likely due to protein-binding effects (Bates *et al*., 1999). The term 'aptamer' (derived from the Latin "aptus", meaning to fit, and "meros", meaning part) was used to describe single stranded DNA or RNA molecules that can selectively bind to a specific target (protein, peptide, carbohydrate, cell, etc.) through the formation of quadruplex structures containing G-quartets. The following figure shows the three-dimensional structure of quadruplex DNA in comparison to the duplex DNA structure.



Source: Bates *et al*., 2010

Aptamers that form quadruplex structures have a number of advantages over non-quadruplex DNA strands as potential therapeutics, including:

- In contrast to unmodified oligonucleotides, which have serum half-lives measured in minutes, the quadruplex structure formed by aptamers make them resistant to nuclease degradation *in vivo* (Dapic *et al*., 2002).

- Quadruplex forming oligonucleotides are efficiently taken up by cells compared to non-quadruplex forms. For example, adding a polyguanine sequence to the 3'-end of an antisense oligonucleotide increased its uptake into J774E cells by 10-fold compared to the oligonucleotide with a 3' polycytosine end (Prasad *et al*., 1999).

AS1411

AS1411 is a DNA aptamer that was discovered serendipitously while investigating the activity of triplex-forming oligonucleotides in cultured prostate cancer cells. It was the 'control' oligonucleotide that shared no complementarity to the target gene (sequence 5′-GGTGGTGGTGGTTGTGGTGGTGGTGG-3'), however it exhibited the highest growth inhibitory characteristics of any oligonucleotide tested. The growth inhibitory effects were found to be independent of triplex formation or any other hybridization-dependent mechanism.

To further investigate the effect of AS1411 on cancer cell growth, the compound was submitted to the Development Therapeutics Program (DTP) at the National Cancer Institute (NCI) and found to exhibit anti-proliferative effects on almost all cancer cell lines while showing little to no toxicity in normal cells at similar concentrations.

Animal studies showed that AS1411 could be administered to rats as a single I.V. infusion over 30 minutes at doses of up to 100 mg/kg and to both rats and dogs as a 96-hour continuous infusion up to 10 mg/kg with no signs of toxicity. Efficacy studies showed activity in xenograft models of non-small cell lung cancer, renal cell carcinoma, and breast cancer.

Mechanistic studies showed that AS1411 binds to nucleolin, a protein that is highly expressed in the nucleoli of proliferating cells but can also be found in the cytoplasm and cell surface (Borer *et al*., 1999; Semenkovich *et al*., 1990). Nucleolin is involved in a number of cellular processes, including rRNA transcription and DNA replication (Srivastava *et al*., 1999). High levels of cytoplasmic and cell surface forms of nucleolin are found in cancer cells, but not in normal cells (Abdelmohsen *et al*., 2012).

AS1411 appears to exert its anti-proliferative effects through multiple mechanisms, including:

- Inhibition of DNA replication, which leads to an altering of the cell cycle such that cells accumulate in S phase (Xu *et al*., 2001).

- It inhibits activation of nuclear factor-kappaB (NF-κB) through association with NF-kB essential modulator (NEMO), which is the regulatory subunit of the inhibitor of kB kinase (IKK) complex (Girvan *et al*., 2006). The NF-kB signaling pathway is involved in a number of cellular responses, including inflammation, cell growth, and apoptosis (Barkett *et al*., 1999; Dolcet *et al*., 2005).

- Alters the location of protein arginine methyltransferase 5 (PRMT5) (Teng *et al*., 2007), PRMT5 is a nucleolin binding protein that controls a number of transcriptional regulatory events through histone methylation, including repression of various tumor suppressor genes (Pal *et al*., 2004).

Clinical Studies of AS1411

AS1411 has been studied in multiple clinical trials as a monotherapy, including a Phase 1 trial in patients with solid tumors and two Phase 2 clinical trials in patients with acute myeloid leukemia (AML) and renal cell carcinoma (RCC).

- The first Phase 1 clinical trial of AS1411 initiated in 2003 and enrolled patients with advanced solid tumors and progressive metastatic disease. A total of 17 patients were enrolled into the trial. Dosing began at 1 mg/kg/day and advanced to 10 mg/kg/day if no toxicity was noted. There were no reports of serious adverse events related to AS1411 administration. One patient with RCC showed a partial response (PR) at four months, which eventually become a complete response (CR) at 11 months. An additional seven patients had disease stabilization for two months or more. (Laber *et al*., 2005).

- An extension of the Phase 1 trial was conducted in patients with RCC and non-small cell lung cancer (NSCLC) (Laber *et al*., 2006). There were no serious adverse events at a dose up to 22 mg/kg/day. Of 5 RCC patients, 1 maintained a CR at 18 months following treatment, three had stable disease (SD), and one had progressive disease (PD). Of three NSCLC patients, one had SD and two had PD.

Based on the positive results seen in the Phase 1 trial, two Phase 2 clinical trials were initiated in patients with RCC and acute myeloid leukemia (AML).

- A total of 37 patients were enrolled in the RCC trial, with 35 of them receiving AS1411 (Rosenberg *et al*., 2014). No serious adverse events were related to AS1411. One patient attained a PR (duration of at least 24 months) and experienced an 84% decrease in the sum diameters of target tumor lesions.

- A total of 71 relapsed/refractory AML patients were randomized in two cohorts (Rizzieri *et al*., 2010). Patients in cohort I were randomized 2:1 to receive 10 mg/kg/day AS1411 IV on Days 1-7 + HiDAC 1.5 g/m^2 bid on Days 4-7 or HiDAC alone for four days. Patients in cohort II received 40 mg/kg/day AS1411 + HiDAC or HiDAC alone. Of 59 patients evaluable for response, the 10 mg/kg/day cohort had 4 CR's (21%), the 40 mg/kg/day cohort had 4 CR's (19%), and the control group had 1 CR (5%).

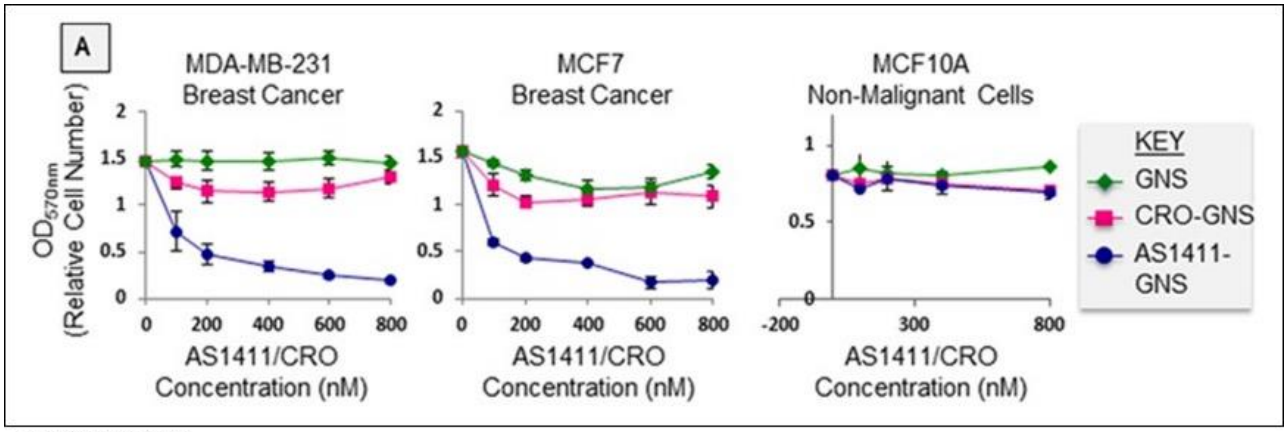
ALAN

While the results from the early clinical trials of AS1411 were encouraging, particularly in AML patients, research was undertaken to determine if AS1411 activity and pharmacology could be enhanced. One of the outcomes of that research was ALAN (Aptatmer-Linked Anti-Nucleolin), an aptamer-based anticancer compound composed of AS1411 attached to gold nanoparticles.

Gold nanoparticles have a number of positive attributes that make them good drug delivery vectors, including a tunable size, a small size that allows them to pass through capillaries efficiently, and for cancer drug deliver they can collect in tumor tissue due to their leaky vasculature (Singh *et al*., 2018).

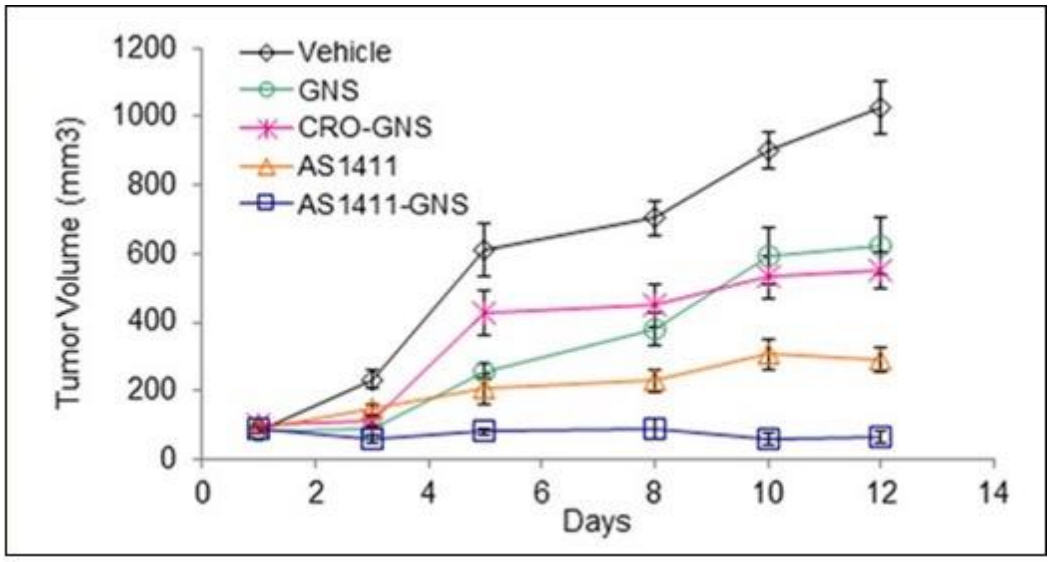
AS1411 was conjugated to 5 nm gold nanoparticles (AS1411-GNS) and found to be stable in aqueous and serum-containing solutions, had superior cellular uptake, and increased antiproliferative effects compared to unconjugated AS1411 (Malik *et al*., 2015).

The following figure shows that increasing concentrations of AS1411-GNS inhibited the proliferation of MDA-MB-231 and MCF-7 breast cancer cells, however there was no effect on the proliferation of MCF10A normal cells. Unconjugated gold nanoparticles (GNS) and gold nanoparticles conjugated to a control aptamer (CRO-GNS) did not have any effect on cell proliferation. This data is important as it shows the cancer-specific effect on cell proliferation for AS1411-GNS.



Source: Malik *et al.*, 2015

In vivo studies were performed in mice that received subcutaneous MDA-MD-231 xenografts. The mice received daily injections for 12 consecutive days with 22 mg oligonucleotides per day (approximately 1 mg/kg/day) of AS1411-GNS, CRO-GNS, or unconjugated AS1411. The following figure shows AS1411-GNS completely inhibited tumor growth and was significantly more effective than the other treatments at equivalent doses ($P<0.05$). In addition, body weight, behavior, and organ histology all indicated that there was no toxicity associated with any of the treatments.



Source: Malik *et al.*, 2015

The company is planning to target acute myeloid leukemia (AML) as a first indication for ALAN based on the encouraging results from the prior Phase 2 clinical trial with AS1411 that saw 20% of patients enter complete remission.

Acute Myeloid Leukemia (AML)

Acute myeloid leukemia (AML) is the most common form of acute leukemia in adults, with approximately 21,000 individuals expected to be diagnosed in the U.S. in 2020 (NCI SEER). It is primarily a disease of older individuals, with the median age of diagnosis being 67 years in the U.S. (DeSantis *et al.*, 2014).

AML is characterized by an abnormal proliferation and differentiation of a clonal population of myeloid stem cells. Large chromosomal rearrangements that result in the production of chimeric proteins can cause the disease through alteration of the normal myeloid maturation process. Genetic mutations are also very common and are seen in >97% of cases (Patel *et al.*, 2012).

Eligible patients (typically younger individuals with good performance status and normal creatinine, albumin, and platelet counts) are usually treated with the "7+3" regimen, consisting of cytarabine for seven days and an anthracycline for the first three days. Approximately 60-80% of patients will achieve complete remission (CR) with induction therapy (Büchner *et al*., 2012). Patients who achieve CR are usually offered consolidation therapy in the form of continued chemotherapy and allogenic hematopoietic stem cell transplantation (HSCT). However, even with a high initial response, the majority of patients will relapse and become refractory to treatment, which leads to a five-year overall survival of only 28%.

Recently Approved AML Therapies

In the past five years there have been a number of new frontline therapies approved for treating AML, including:

- **Rydapt® (midostaurin)**: Rydapt was approved in 2017 for the treatment of newly diagnosed AML with a FLT3 mutation. The drug generated revenues of $120 million in 2019 (EvaluatePharma). It was approved based upon the results of a Phase 3 clinical trial that showed it significantly increased overall survival (HR 0.78; *P*=0.009) and event-free survival (HR 0.78; *P*=0.002) in newly diagnosed AML patients with a FLT3 mutation (Stone *et al*., 2017). Midostaurin is a multi-targeted protein kinase inhibitor with an IC50 < 10 nM in Ba/F3 cells expressing mutant FLT3 (Weisberg *et al*., 2002).

- **Vyxeos® (daunorubicin and cytarabine)**: Vyxeos was approved in 2017 for the treatment of newly diagnosed AML and generated revenues of $121 million in 2019 (EvalutePharma). It is a liposomal formulation of the "7+3" regimen and was approved based on a Phase 3 trial that showed it significantly improved median overall survival compared to standard "7+3" therapy in newly diagnosed AML patients age 60 to 75 (Lancet *et al*., 2018).

- **Venclexta® (venetoclax)**: Venclexta was approved in 2018 for the treatment of newly diagnosed AML when used in combination with azacytidine, decitabine, or low-dose cytarabine in patients age 75 years or older. The drug received accelerated approval in 2018 based on the results of Phase 1/2 trials and in 2020 AbbVie announced positive results from confirmatory Phase 3 clinical trials. In 2019, it generated revenues of $69 million, however it is forecast to generate approximately $1.4 billion by 2026 (EvaluatePharma).

- **Xospata® (gilteritinib)**: Xospata was approved in 2018 for the treatment of relapsed or refractory AML with a FLT3 mutation. It generated revenues of $132 million in 2019 (EvaluatePharma). The drug was approved based on results of a Phase 3 clinical trial that showed it significantly increased overall survival compared to salvage chemotherapy (Perl *et al*., 2019).

- **Tibsovo® (ivosidenib)**: Tibsovo was approved in 2019 for the treatment of newly diagnosed AML with a susceptible IDH1 mutation in patients at least age 75. It was approved based on the results of an open label, single arm, multicenter clinical trial (DiNardo *et al*., 2018). In 2019 it generated revenues of approximately $60 million.

Clinical Plan

Qualigen is currently finalizing the formulation for ALAN (which may include PEGylation to increase the half-life of the drug) such that IND-enabling studies can commence, including PK and toxicology studies. We anticipate Phase 1 clinical trials initiating in 2021.

AS1411 as an Anti-Viral Agent

The current COVID-19 pandemic caused by the novel SARS-CoV-2coronavirus has disrupted life for virtually everyone and a number of biopharmaceutical companies are developing treatments and vaccines to combat the epidemic. Thus far, Gilead's remdesivir is the only anti-viral compound to receive

emergency use authorization from the FDA for treating SARS-CoV-2 infection, although its results were not particularly impressive (Beigel *et al*., 2020). Most of the COVID-19 therapies in development are targeting complications of SARS-CoV-2 infection, such as acute respiratory distress syndrome (ARDS), or on vaccines to prevent infection. Thus, there exists a significant need for new anti-viral therapies that can be utilized to treat or prevent infection with SARS-CoV-2.

In addition to its use in oncology, AS1411 has also exhibited antiviral activity in a number of different *in vitro* assays against different viruses. The following manuscripts show that AS1411 is active against a number of different RNA viruses, including dengue virus, human immunodeficiency virus (HIV), and respiratory syncytial virus (RSV). We believe this is important as Qualigen will be pursuing the use of AS1411 as a therapeutic for SARS-CoV-2 infection, and that the following studies provide proof-of-concept for AS1411 as an anti-viral agent and nucleolin as an antiviral target.

- Balinsky *et al*., 2013: The dengue virus capsid protein is a structural component of the infectious virion, and it interacts with and colocalizes with nucleolin. Both knockdown of nucleolin expression with siRNA and treatment with AS1411 caused a significant reduction in viral titers following dengue virus infection. There was no change in viral RNA or protein levels at early time points post-infection, thus nucleolin is likely involved in viral morphogenesis.

- Perrone *et al*., 2016: Cell-surface nucleolin is a low-affinity co-receptor for HIV on target cells, thus since AS1411 binds to nucleolin it was tested as a potential anti-HIV therapy. AS1411 inhibited HIV attachment and entry into target cells along with antiviral activity without displaying cytotoxicity.

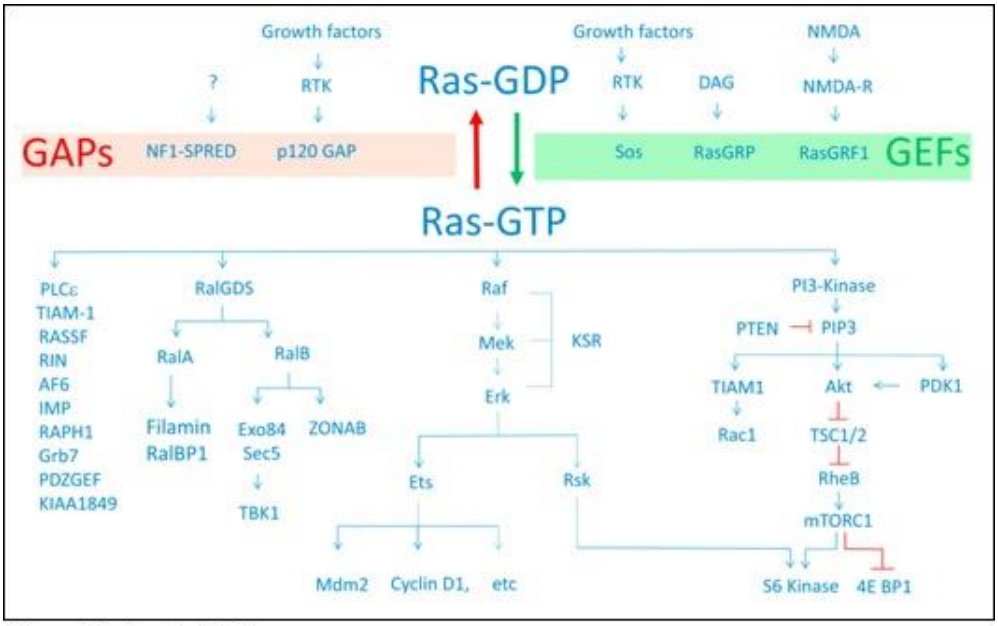
- Mastrangelo *et al*., 2017: Following administration of AS1411 to RSV-infected mice and rats there was a reduction in lung viral titers, decreased airway inflammation, and decreased IL-4/IFN-g ratios compared to untreated, infected animals.

Qualigen is planning to conduct a clinical trial in approximately 500 patients suffering from SARS-CoV-2 infection, and while the final details have yet to be decided on we believe it will encompass multiple treatment arms (AS1411 alone, AS1411 plus standard of care, standard of care alone) and examine endpoints at approximately 10 days. Given that Gilead performed a clinical trial of remdesivir in 1,060 SARS-CoV-2 patients in a couple of months means that the trial could likely be performed relatively quickly. We anticipate the company initiating a Phase 1/2 clinical trial early in 2021.

RAS-F

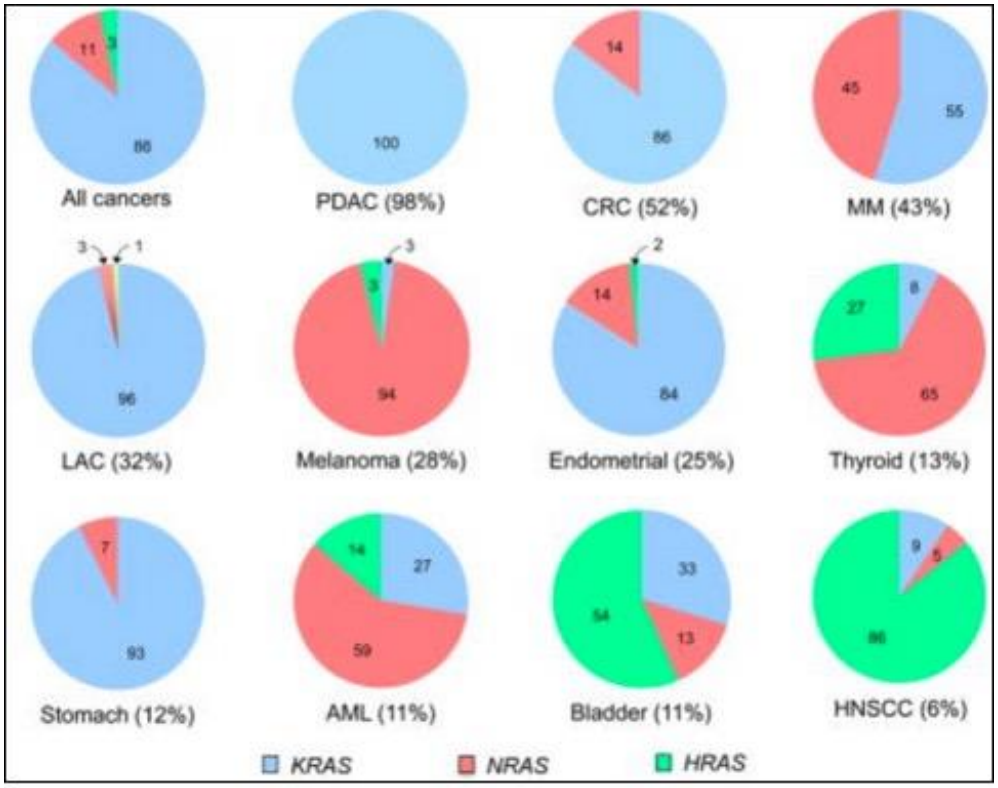
In July 2020, Qualigen announced an agreement with the University of Louisville for intellectual property covering the “RAS-F” family of RAS protein-protein interaction inhibitor small molecule drug candidates. The company is currently evaluating this group of compounds to identify a lead development candidate as a therapeutic against a range of cancers.

There are three human RAS genes (*HRAS*, *KRAS*, and *NRAS*) that encode four similar RAS proteins that function as transducers to connect cell surface receptors with intracellular signaling pathways (Pylayeva-Gupta *et al*., 2011). The RAS proteins cycle between an “on” and “off” state depending on whether they are bound to GTP (“on”) or GDP (“off”). The transition between the “on” and “off” states is typically controlled by guanine nucleotide exchange factors (GEFs), which stimulate exchange of GDP for GTP, and by GTPase-activating proteins (GAPs), which stimulate RAS-mediated GTP hydrolysis (Stephen *et al*., 2014). RAS-GTP binds to and activates a number of different downstream signaling pathways, including those involved in proliferation, apoptosis, and metabolism. The following image shows a simplified overview of the RAS pathway, GAPs and GEFs that control RAS function, and examples of downstream effectors to which RAS-GTP binds.



Source: Stephen *et al.*, 2014

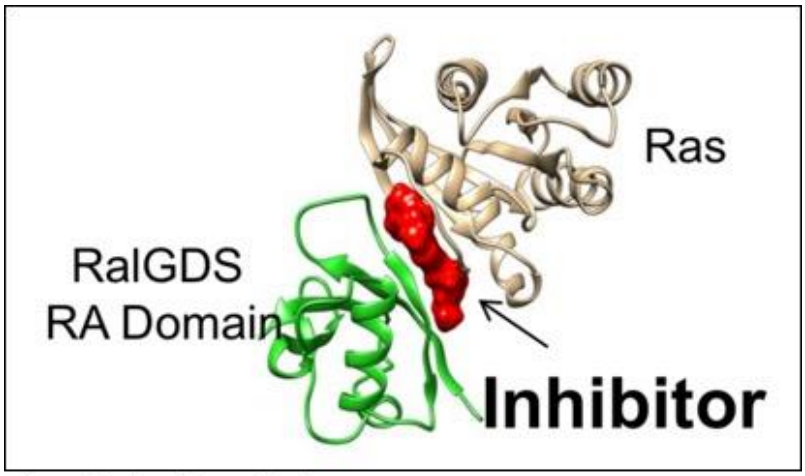
RAS mutations are found at varying rates across many different types of cancers, with *KRAS* mutations found most frequently (86%) followed by *NRAS* (11%) and *HRAS* (3%), with the overall range of any RAS mutation occurring in approximately 9-30% of all tumor samples sequenced (Cox *et al.*, 2014). The following figure shows the distribution of RAS mutations across 11 different tumor types, with *KRAS* mutations occurring most frequently in pancreatic ductal adenocarcinoma (PDAC), lung adenocarcinoma (LAC), and colorectal cancer (CRC); *NRAS* mutations are seen most frequently in melanoma, thyroid cancer, and AML; and *HRAS* mutations are seen most frequently in head and neck small cell carcinoma (HNSCC) and bladder cancer.



Source: Cox *et al.*, 2014

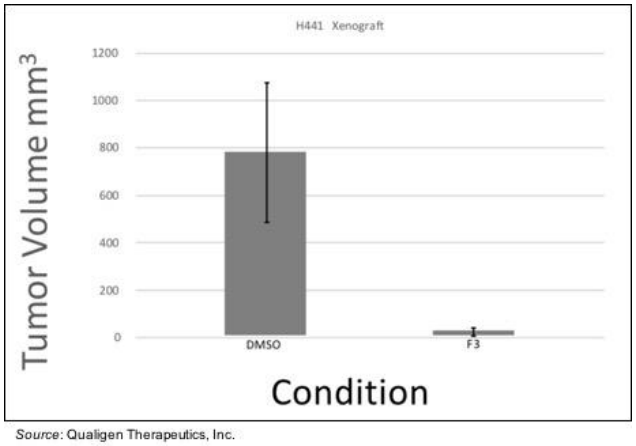
RAS mutations interfere with the ability of GAP to perform GTP hydrolysis and thus RAS is maintained in the RAS-GTP “on” state and continuously exerts its downstream effects through binding of effector proteins such as Raf, RalGDS, and PI3K. While drugs have successfully been designed for protein kinases that bind ATP (e.g., erlotinib, ibrutinib, etc.), efforts to develop GTP-competitive small molecule inhibitors of RAS have been unsuccessful thus far since GTP binds with picomolar affinity to RAS, compared with the low micromolar affinity between ATP and protein kinases. Thus, alternative strategies may be necessary to develop effective RAS inhibitors.

In an effort to develop a treatment for RAS-driven cancer, researchers at the University of Louisville screened a library of two million compounds to identify small molecules that would inhibit the protein-protein interaction between RAS and effector proteins, rather than targeting the GTP binding domain of RAS. The following image shows how an inhibitor molecule could block the interaction between RAS and an effector protein (e.g., RalGDS).



Source: Qualigen Therapeutics, Inc.

A RAS-binding compound, termed F3, was identified and shown to inhibit RAS effector interactions, induce apoptosis in cells cultured in 3D with no effect on cells in normal 2D culture, and inhibit tumor formation in a xenograft model without toxicity. Mice were injected with NCI-H441 lung tumor cells and 48 hours later were injected i.p. with 20 mg/kg F3 every other day for four weeks. The following graph shows that F3 treatment almost completely blocked tumor formation compared to mice treated with DMSO.



Source: Qualigen Therapeutics, Inc.

Clinical Plan

Qualigen is in the process of identifying a lead development compound from the RAS-F library and we anticipate compound selection and IND-enabling studies to initiate in 2021 such that a Phase 1 clinical trial can initiate in 2022.

Other RAS Targeted Agents in Development

While previously thought to be "undruggable", in 2013 it was shown that the $KRAS^{G12C}$ mutation resulted in the formation of a previously unknown allosteric binding pocket near the nucleotide binding site on the protein (Ostrem *et al*., 2013). A series of compounds were identified that could covalently bind to the cysteine residue and keep KRAS in its inactive GDP-bound state. Two of these compounds are now in clinical development.

- **AMG 510 (sotorasib)**: This compound is being developed by Amgen Inc. (AMGN) and was the first $KRAS^{G12C}$ inhibitor to enter clinical development (Canon *et al*., 2019). In preclinical studies, AMG 510 treatment led to the regression of $KRAS^{G12C}$ tumors and worked in concert with chemotherapy and other targeted agents. The compound is currently being studied in the CodeBreaK clinical trial program, and Amgen recently presented data at the ASCO20 Virtual Scientific Program showing an overall response rate (ORR) of 12% and a disease control rate (DCR) of 80% in 25 patients with advanced CRC. Data from a potentially registrational Phase 2 trial in non-small cell lung cancer (NSCLC) is expected before the end of 2020, with data from the Phase 2 trial in CRC expected in early 2021.

- **MRTX849**: This compound is being developed by Mirati Therapeutics (MRTX). It was derived from a tetrahydropyridopyrimidine compound that exhibited good anti-tumor activity but had multiple pharmacokinetic limitations (Fell *et al*., 2020). Mirati presented the first clinical data for MRTX849 at the 2019 AACR-NCI-EORTC conference showing three of five evaluable NSCLC patients and one of two CRC patients achieved a partial response, with the remaining patients experiencing stable disease. The compound is currently studied in two Phase 1/2 clinical trials both as a monotherapy and in combination with targeted agents.

In addition to direct KRAS targeting agents, indirect targeting of KRAS using various drug combinations is also being tested. Cardiff Oncology (CRDF) is developing onvansertib, a selective inhibitor of pololike kinase 1 (PLK1), a serine/threonine kinase that regulates mitotic progression. Upregulation of PLK1 in CRC patients is associated with poor overall survival and more advanced disease stages (Ran *et al*., 2019), while a genome-wide RNA interference screen found that PLK1 has synthetic lethal interactions with KRAS, meaning that KRAS-mutant cells are more sensitive to PLK1 inhibition (Luo *et al*., 2009). Recent results from Cardiff showed that 7 of 8 evaluable CRC patients showed either a partial response or stable disease and a median progression-free survival of at least 6.5 months. One patient from the study has gone on to have successful curative surgery.

FastPack®

The company's FastPack diagnostic system in a proprietary platform that provides rapid and accurate immunoassay testing results. It consists of the FastPack Analyzer and FastPack test pouches that includes a single-use, disposable foil packet containing the FastPack reagent chemistry. The company currently markets 10 assays, including tests for prostate cancer, thyroid function, metabolic disorders, and research applications. FastPack products are now available in approximately 1,000 physician offices worldwide. Since launching in 2001, cumulative sales of FastPack products has exceeded $100 million.

Qualigen recently announced it has begun commercial shipments of a diagnostic test for SARS-CoV-2 IgG antibodies. The company has submitted the test to the U.S. FDA for emergency use authorization (EUA) and has also submitted an official notification to the FDA of its plan to exercise its right to sell the test while EUA is pending. The COVID-19 antibody test is designed to be used with the new FastPack PRO System, which is an upgraded version of the FastPack Analyzer.

While Qualigen will continue to sell FastPack products through its distribution partner Sekisui, the main focus of the company will be on the development of therapeutics for cancer and infectious diseases.

STARS™

The same core technologies that were developed for the FastPack system are the basis for the company's expansion into a therapeutic application for removing disease associated agents from a patient's blood, the Selective Target Antigen Removal System (STARS). STARS consists of a membrane targeted with a capture reagent inside of a cartridge and are expected to be used with conventional dialysis and hemofiltration machines. Examples of agents that could potentially be removed with STARS include immune checkpoints, metastatic cells, and inflammatory factors. STARS could also potentially be used to treat infectious diseases by removing circulating viruses. The company is beginning development of STARS with clinical trials expected to start in 2023.

Financial Update

On August 14, 2020, Qualigen announced financial results for the first quarter of fiscal year 2021 that ended on June 30, 2020. Total revenues for the three months ending June 30, 2020 were $0.9 million compared to $1.5 million for the same period in 2019. The decrease was primarily due to the COVID-19 pandemic, which resulted in a decreased number of patient visits to physician offices, clinics, and small hospitals. All revenue was derived from the sale of diagnostic products.

G&A expenses for the first quarter of fiscal year 2021 were $2.0 million compared with $0.3 million for the first quarter of fiscal year 2020. The increase is primarily due to one-time expenses associated with the reverse merger and other public company expenses. R&D expenses for the three months ending June 30, 2020 were $0.6 million compared to $0.7 million for the prior-year period. The decrease was primarily due to the absence of related-party research and development costs associated with diagnostic development projects with Sekisui Diagnostics, LLC offset by higher expenses related to sponsored research at the University of Louisville and COVID-19 antibody diagnostic test development.

Net loss for the first quarter of fiscal year 2021 was $18.6 million, or $2.12 per share, compared with a net loss of $0.6 million, or $0.11 per share, for the first quarter of fiscal year 2020. However, the net loss in the most recent quarter included a non-cash charge of $16.2 million for the fair value of warrant liabilities. Loss from operations for the three months ending June 30, 2020 was $2.6 million compared to $0.5 million for the months ending June 30, 2019.

As of June 30, 2020, Qualigen had approximately $2.3 million in cash and cash equivalents. Subsequent to the end of the quarter, the company raised approximately $18 million in gross proceeds from two registered direct equity offerings in July and August.

MANAGEMENT PROFILES

Michael Poirier – President, Chief Executive Officer, and Chairman

Mr. Poirier founded Qualigen in 1996 and is its Chairman, President, and Chief Executive Officer. Prior to founding Qualigen, Mr. Poirier was Vice President of Marketing for Ashirus Technologies, Inc., a Minneapolis-based manufacturer of innovative high-precision dispensing pumps and related equipment for the medical industry. From 1993 to 1995, Mr. Poirier was Director of US Area Operations for EnSys, Inc., located in Research Triangle, North Carolina. EnSys developed and manufactured field-portable immunoassay test kits for the environmental remediation industry. From 1991 to 1993, Mr. Poirier was employed by Sanofi Pasteur in Chaska, Minnesota, as a Marketing Manager responsible for launching the ACCESS® Immunoassay System. This novel diagnostic system was later acquired by Beckman-Coulter and is now one of the leading immunoassay test systems worldwide. From 1985 to 1991, Mr. Poirier was employed by Abbott Diagnostics, a division of Abbott Laboratories, Inc. in various marketing and sales positions, including Worldwide Immunoassay Product Manager for the IMx® and AxSym® immunoassay diagnostic systems. Both IMx and later, AxSym, became the leaders in their respective markets. Prior to working at Abbott, Mr. Poirier served as an officer in the United States Navy, assigned to the US Atlantic Fleet. Mr. Poirier holds a B.A. from Providence College and attended the University of Zürich, Switzerland, School of Law.

Christopher Lotz – Chief Financial Officer

Mr. Lotz joined Qualigen as Director of Finance in 2002 and was appointed Vice President and Chief Financial Officer in 2003. Prior to joining Qualigen, Mr. Lotz was Director of Finance for the United States subsidiaries of Bexcom, a procurement management software company based in Singapore from 1999 to 2001. From 1998 to 1999 Mr. Lotz served as Controller of California Furniture Collections, Inc. a custom furniture manufacturer, and from 1987 to 1998 Mr. Lotz was Controller and then Vice President and Chief Financial Officer of Group Publishing, Inc. a book and magazine publisher. Mr. Lotz holds a B.S. in Business Administration from Colorado State University.

Shishir Sinha – Vice President, Operations, Corporate Secretary

Mr. Sinha joined Qualigen as Vice President, Operations & QA/QC in 2006 and was appointed Corporate Secretary in 2017. Prior to joining Qualigen, Mr. Sinha held leadership roles in the molecular diagnostics industry including Director of Manufacturing for Nanogen, and Senior Manager of Oligonucleotide Manufacturing for Celera Diagnostics from 2004-2006. From 2001-2004, Mr. Sinha served as Director of Manufacturing for Sequenom, a developer of industry leading methods and equipment to analyze DNA. Mr. Sinha was Packaging Manager for Sandoz Pharmaceutics (Novartis) from 2000-2001, and from 1989 to 2000 held various management positions in QC, manufacturing, planning and production control with Microgenics Corp, a manufacturer of immunoassay diagnostic kits. Mr. Sinha holds an MBEE in Biotechnology Enterprise from John Hopkins University and B.A. in Genetics from the University of California, Berkeley.

Wajdi Abdul-Ahad, PhD – Vice President, R&D, Chief Scientific Officer

Dr. Abdul-Ahad is Qualigen's Vice President of Research and Development and Chief Scientific Officer. Since joining the Company in 2006, he has successfully developed and commercialized numerous complex immunoassays on both the FastPack and FastPack IP Systems. In addition, Dr. Abdul-Ahad is responsible for all surface coating, nanotechnology and reagent manufacturing, as well as integration of new drug manufacturing systems and processes. Prior to joining Qualigen, Dr. Abdul-Ahad led multifunctional design teams at Beckman Coulter that developed and commercialized over 15 assays on their industry leading Access and Synchron automated systems. From 1988 to 1990, Dr. Abdul-Ahad held various management positions with the National Diagnostics Center and Noctech, Inc., both located in Galway, Ireland. Dr. Abdul-Ahad holds a PhD in Biochemistry from National University of Ireland, Galway; an MS in Clinical Chemistry from the University of Surrey, England; an MBA from the University of La Verne, California and a BS in Pharmacy from the University of Baghdad, Iraq. He also holds certifications and licenses from the American Board of Clinical Chemistry, State of California (Registered Pharmacist), National Registry of Clinical Chemistry and the National Academy for Clinical Biochemistry. Dr. Abdul-Ahad's professional affiliations include the Association of Clinical Biochemistry (ACB-UK), the American Association for Clinical Chemistry and the American Pharmaceutical Association. Dr. Abdul-Ahad is also the author or co-author of numerous scientific publications.

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VALUATION

We are initiating coverage of Qualigen Therapeutics, Inc. with a valuation of $10.00. Qualigen is a biopharmaceutical company developing novel treatments for cancer and infectious diseases while continuing and expanding its FDA approved FastPack® System. The company's development pipeline includes ALAN, featuring a DNA aptamer (AS1411) linked to a gold nanoparticle, RAS-F, a family of small molecule RAS protein-protein interaction inhibitors, and STARS™, a treatment device product designed to remove various compounds from circulating blood. AS1411 is also being developed as a potential treatment for SARS-CoV-2 infection. The company also markets the FDA approved FastPack System, which includes diagnostic instruments and test kits. Qualigen recently began shipment of a SARS-CoV-2 IgG diagnostic test for COVID antibodies. The FastPack product line is sold worldwide by its commercial partner Sekisui Diagnostics, LLC.

Valuation

We value Qualigen using a probability adjusted discounted cash flow model that takes into account potential future revenues for AS1411, ALAN, RAS-F, and FastPack.

For AS1411 as an antiviral, we model for the company to initiate a clinical trial in COVID-19 in the first half of 2021 and to receive emergency use authorization and begin selling the drug in 2022 (fiscal year 2023). We also anticipate the company testing AS1411 as an antiviral for other indications such as influenza. We model for peak sales of AS1411 as an antiviral of $100 million. Using a 15% discount rate and a 25% probability of approval leads to a net present value for AS1411 as an antiviral of $10 million.

For ALAN, we model for a Phase 1 trial to initiate in 2021, an NDA filing in 2026, and approval in 2027. We model for peak worldwide sales of approximately $2 billion and for the company to receive 15% royalties on net sales. Using a 15% discount rate and a 33% probability of approval leads to a net present value for ALAN in AML of approximately $68 million. In addition, we value additional potential indications for ALAN at $100 million.

For RAS-F, we model for the company to first develop a drug for pancreatic cancer. We estimate a Phase 1 clinical trial will initiate in 2022 with an NDA filing in 2027 and approval in 2028. We model for worldwide peak sales in pancreatic cancer of approximately $2 billion and for the company to receive 15% royalties on net sales. Using a 15% discount rate and a 20% probability of approval leads to a net present value for RAS-F in pancreatic cancer of $38 million. In addition, we value additional indications for RAS-F at $100 million.

Combining the net present value for the company's development pipeline along with the company's current cash position, the cash from warrant exercises, and a $50 million valuation for FastPak leads to a combined value of approximately $400 million. Dividing by the fully diluted share count of approximately 40.7 million leads to a valuation of approximately $10 per share.

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PROJECTED FINANCIALS

Qualigen Therapeutics, Inc.	FY2020 A	Q1FY21 A	Q2FY21 E	Q3FY21 E	Q4FY21 E	FY2021 E	FY2022 E	FY2023 E
ALAN	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
AS1411	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$1.5
RAS-F3	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
STARS	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
FastPack	$5.5	$0.9	$1.0	$1.2	$1.3	$4.4	$5.5	$6.3
Other Income	$0.1	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Total Revenues	**$5.6**	**$0.9**	**$1.0**	**$1.2**	**$1.3**	**$4.4**	**$5.5**	**$7.8**
Cost of Sales	$4.0	$0.8	$0.7	$0.8	$0.9	$3.2	$4.0	$4.5
Product Gross Margin	*28%*	*11%*	*30%*	*33%*	*31%*	*27%*	*27%*	*42%*
Research & Development	$1.2	$0.6	$0.7	$0.8	$0.9	$3.0	$7.0	$11.0
Selling and Marketing	$0.4	$0.1	$0.1	$0.1	$0.1	$0.4	$0.5	$0.8
General & Administrative	$1.5	$2.0	$2.1	$2.2	$2.4	$8.7	$10.0	$11.0
Other (Income) Expense	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Operating Income	($1.5)	($2.6)	($2.6)	($2.7)	($3.0)	($10.9)	($16.0)	($19.5)
Operating Margin	-	-	-	-	-	-	-	-
Non-Operating Expenses (Net)	($0.3)	$16.0	($0.5)	($7.0)	($8.5)	$0.0	($0.3)	($0.3)
Pre-Tax Income	($1.8)	($18.6)	($2.1)	$4.3	$5.5	($10.9)	($15.7)	($19.2)
Income Taxes	$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	**($1.8)**	**($18.6)**	**($2.1)**	**$4.3**	**$5.5**	**($10.9)**	**($15.7)**	**($19.2)**
Net Margin	-	-	-	-	-	-	-	-
Reported EPS	**($0.32)**	**($2.12)**	**($0.10)**	**$0.20**	**$0.26**	**($0.61)**	**($0.63)**	**($0.69)**
YOY Growth	-	-	-	-	-	-	-	-
Basic Shares Outstanding	5.6	8.7	21.0	21.0	21.0	17.9	25.0	28.0

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

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