Zacks Small-Cap Research

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Aevi Genomic Medicine (GNMX-NASDAQ)

GNMX: Name Change To Aevi Genomic Medicine, Inc

Given the early stage of GNMX we continue to value the company using DCF model based on annual revenue of an "average" orphan drug. See the end of this report for a detailed explanation of our model inputs. We continue to see fair value at approximately $350M or ~$10/share. Further successful progression through the development pathway should provide for additional de-risking and potential upside to our current $10/share target price.

Current Price (12/23/16)	$5.27
Valuation	**$10.00**

OUTLOOK

Recent neuroFix acquisition brought high-potential NFC-1 candidate. Ph 1 data looks very encouraging. This could move rapidly through development and be the first commercialized product - could address both ADHD and orphan indications. Highly positive results of a phenotyping/genotyping study. Next few months looks to be potentially exciting as initial read-outs from both the NFC-1 ADHD and 22q11.2 Deletion Syndrome studies are slated to happen in near-term. If the planned phase 2/3 ADHD study (top-line data expected Q1 2017) confirms what was demonstrated in phase 1, we think this could be a needle-mover to the share price.
Most recent program to come online is first-in-class monoclonal antibody targeting ultra-orphan indication Severe Pediatric Onset Inflammatory Bowel Disease. Also de-risked to an extent. POC results in 1H 2017. Could add $300M+ market opportunity.

SUMMARY DATA

52-Week High	**$6.85**
52-Week Low	**$3.18**
One-Year Return (%)	**-12.26**
Beta	**1.17**
Average Daily Volume (sh)	**174,203**
Shares Outstanding (mil)	**37**
Market Capitalization ($mil)	**$202**
Short Interest Ratio (days)	**N/A**
Institutional Ownership (%)	**44**
Insider Ownership (%)	**23**
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 2016 Estimate	**N/A**
P/E using 2017 Estimate	**N/A**
Zacks Rank	**N/A**

Risk Level	**Above Avg.,**
Type of Stock	**Small-Growth**
Industry	**Med-Biomed/Gene**

ZACKS ESTIMATES

Revenue
(in '000s of $)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2015	0 A	0 A	0 A	0 A	0 A
2016	0 A	0 A	0 A	0 E	0 E
2017					0 E
2018					0 E

Earnings per Share

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2015	-$0.36 A	-$0.24 A	-$0.66 A	-$0.25 A	-$1.51 A
2016	-$0.34 A	-$0.35 A	-$0.29 A	-$0.31 E	-$1.28 E
2017					-$1.17 E
2018					-$1.02 E

Zacks Projected EPS Growth Rate - Next 5 Years % **N/A**

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Name / Ticker Change Effective December 16th

We are republishing our most recent report to reflect the company's name and ticker change to Aevi Genomic Medicine, Inc / GNMX. The company notes that Aevi means "life story" in an Old Norse language and is reflective of their mission of improving lives of children and adults with pediatric onset life-altering diseases.

Management Now Guiding for Ph 2/3 mGluR+ADHD Data in Q1 2017…

On the operational front, progress continues on the two NFC-1 programs (ADHD and 22q) with recent highlights including presentation of the mGluR+ADHD geno/pheno at AACAP in October, commencement of enrollment of the phase II/III interventional study (adolescents, n=90) and initiation of the 22q Deletion Syndrome signal finding study. Management now expects to have initial data from the ADHD interventional study in Q1 2017 (slightly delayed from Q4 2016) and from the open-label portion of the 22q signal finding study in 1H 2017. And with the IND transferred and Type B meeting with FDA completed, GNMX now has the initial groundwork laid for the anti-LIGHT program to commence.

The slight delay in expected top-line data for Ph II/III mGluR+ADHD is likely a result of slower enrollment due to the holiday season. As the non-interventional study enrolled extremely rapidly and is feeding this Ph II/III interventional study, we think it's reasonable to expect that post-New Years, the pace of enrollment will return to prior expectations.

Expected upcoming milestones include;

NFC-1:

- mGluR+ ADHD phase II/III adolescent top-line data in Q1 2017
- 22q enrollment began in October. Expect open-label (through first 5 weeks) responder data in 1H 2017

anti-LIGHT:

- signal finding study commences Q4 2016
- initial open label responder data in 1H 2017

NFC-1: Confirmed mGluR+ Mutation Rates, Phase II/III Initiated. Could Be Fast-Moving Through Ph III

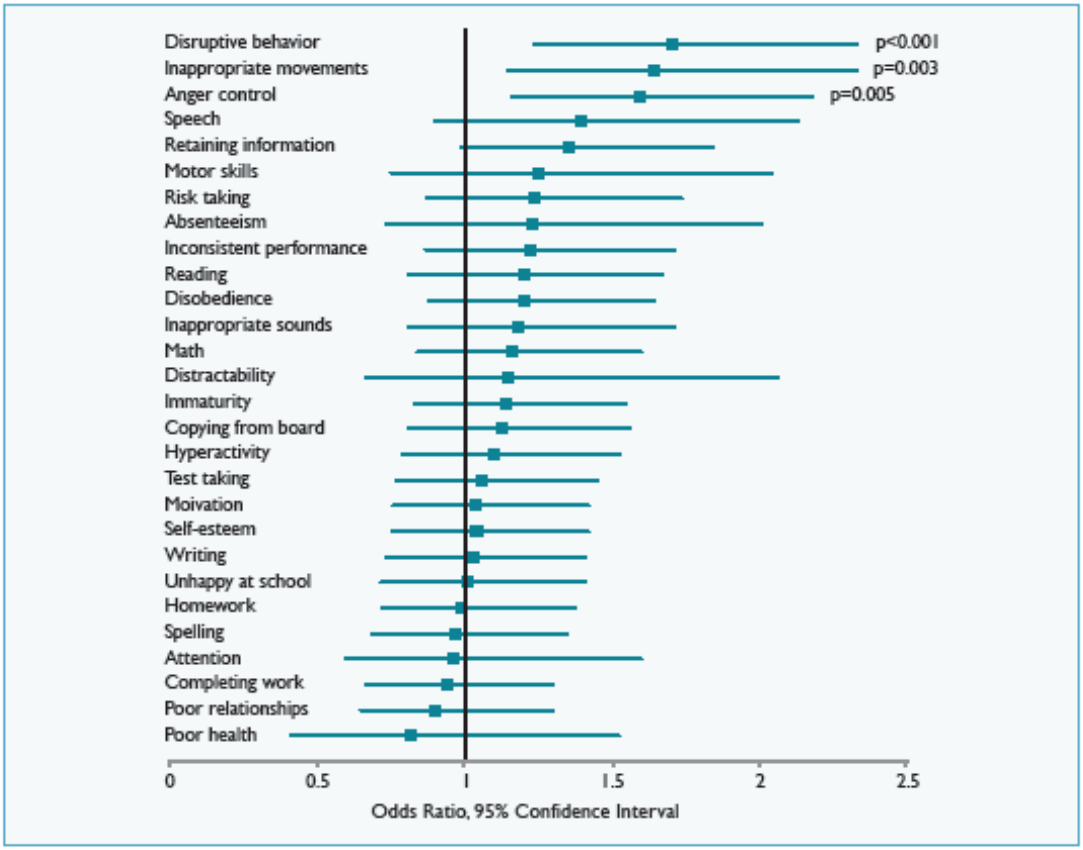
Results of the non-interventional phenotype/genotype study are exactly what management was hoping for. Results to-date (the study is ongoing) were presented at AACAP in October on the first 1,013 subjects which showed about 26% of patients ages 6 – 12 and 20% of patients ages 12 – 17 tested positive for genetic mutations that affect the mGluR network (table below from October AACAP Poster Presentation). Since then analysis has been done on over 1,500 patients in this study which has indicated prevalence is approximately 26% in ages 6 – 12 and 21% in ages 12 – 17 years. This is actually slightly higher (i.e. better) than earlier research by Dr. Hakonarson which indicated ~20% of ADHD patients have an underlying mGluR network mutation.

	Age		
Mutation Status	**6 - <12 yrs**	**12 - 17 yrs**	**Total**
Positive, N (%)	75 (26%)	145 (20%)	220 (22%)
Negative, N (%)	216 (74%)	577 (80%)	793 (78%)
Total, N	291	722	1013

SOURCE: GNMX AACAP 2016 Poster Presentation

The October AACAP presentation also included new data not previously announced including some interesting observations related to phenotypic traits among patients with mGluR mutations. It was found that ADHD patients with mGluR network mutations were significantly more likely to have disruptive behaviors, inappropriate movements, and anger control issue as compared ADHD patients without mGluR network mutations (see graphic below).

Association Between Absence/Presence of Mutations in *GRM* Network Genes and Behavioral Concerns



- ADHD patients with *GRM* network mutations significantly more likely to have disruptive behaviors, inappropriate movements, and anger control issues vs. ADHD patients without genetic disruptions of glutamate signaling.

SOURCE: GNMX AACAP 2016 Poster Presentation

The study also had a somewhat unexpected outcome as well – that being the very rapid pace of enrollment. Prior to the start of the pheno/geno study management had expected it would likely run through approximately the end of 2016. Instead it took less than four months for the initial 1,000+ patients to run through. Management attributes the rapid pace to the current lack of safe and effective ADHD treatments which has created a thirst from ADHD sufferers, their parents and clinicians for a better alternative. This is indicative of the 95%+ of subjects in the geno/pheno study which agreed to be on a call-back list for inclusion in future studies, including GNMX's phase II/III ADHD study. Enrollment in the phase II/III interventional study began in June with top-line data expected by the end of Q1 2017.

The phase II/III mGluR+ADHD randomized, placebo-controlled study in adolescents (ages 12 – 17) dubbed the SAGA (Study of Adolescent Glutamate Receptor Network Copy Number Variant ADHD) trial;

- enrollment (n=90), first patient enrolled in June
- will use same 23 trial sites as geno/pheno study
- randomize 1:1; NFC-1/placebo
- following wash-out period patients will
    - receive placebo or
    - receive NFC-1
        - in weekly escalating doses from 100mg (twice/day) to 400mg based on tolerability
        - after the 4th week patients will stay on the optimized dose for 2-week maintenance phase
        - followed by 1 week off-drug for safety observation
- Response endpoints will be ADHD RS (parent assessment) and Clinical Global Impressions (CGI-I)

- as typical stimulant-based ADHD drugs are associated with significant side effects including anxiety and difficulty sleeping, this study will also assess sleep using adolescents sleep hygiene scale (ASHS) and anxiety with the screen for childhood anxiety related disorders (SCARED)

Management believes this study can also enroll rapidly, facilitated by the 95% of subjects in the pheno/geno study that indicated interest in continuing in future studies. GNMX expects top-line results to be available in Q1 2017.

Phase III
Assuming positive results, they would then move to phase III studies – currently the expectation is to conduct both a pediatric and adolescent phase III study. Specifics on size and design will be determined following conclusion (and results of) the phase II/III study.

GNMX will also be developing a companion diagnostic which will determine whether an individual is positive for the genetic mutations of interest and, therefore, appropriate for treatment with NFC-1. While specifics are still in the planning stage, that this is expected to follow an FDA-clearance pathway (i.e. – will not be an LDT).

22q11.2 Deletion Syndrome
While initiation of the 22q phase I/II study was delayed due mostly to administrative issues at CHOP, the study finally initiated in September and enrollment began in October. Management noted on the Q3 call that enrollment has been progressing slowly due to the characteristically "fragile" nature of patients with this disorder. The delay to initiating the study along with slower than expected enrollment has pushed back the timeline for initial read-out from Q4 of this year to the first half of 2017. The randomized, placebo-controlled, proof-of-concept, dose-finding study is a single-site study at CHOP;

- enroll (n=30) adolescents (ages 12 – 17). First patient entered study in October
- protocol;
    - open label, dose-finding phase for first 5 weeks
    - non-responders will exit the study. Responders will be randomized ~1:3; NFC-1/placebo
        - will remain on optimal dose for up to 7 weeks
- assessments will be made on three neuropsychiatric disorders; ADHD, anxiety and autism spectrum disorders
    - endpoints will be CGI-I, ADHD-RS, Pediatric Anxiety Rating Scale (PARS) and Childhood Autism Rating Scale (CARS-2)
- data from open label portion (through first 5 weeks) in 1H 2017

GNMX noted that they do not expect much in the way of a placebo response given the typical relatively low (~65 – 75) IQ of 22q subjects. As such, we think that there's potential for a marked signal despite the small size of this study.

Severe Pediatric Onset Inflammatory Bowel Disease Program. Second CHOP Collaboration
In June GNMX announced that, in collaboration with Japanese biopharmaceutical company Kyowa Hakko Kirin, they initiated a development program with an anti-LIGHT monoclonal antibody for the ultra-orphan disease Severe Pediatric Onset Inflammatory Bowel Disease. This is the second program from the company's research collaboration with CHOP. It will leverage CHOP's Center for Applied Genomics (CAG), one of the world's largest repositories of pediatric genetic data.

Key points include;

- Phase 2-ready first-in-class biologic with available clinical supply
- GNMX will initiate (Q4 2016) signal finding study with Dr. Robert Baldassono, CHOP's Director for the Center of Pediatric IBD
- Kyowa Hakko Kirin has ~$3B in annual sales with focus on discovering antibody related drugs. Existing collaborations with large pharma include mogamulizumab (anti-CCR4) and benralizumab (anti-IL-5R alpha). Other collaborations include anti-FGF23a and anti-CD40 monoclonal antibodies
- Upon successful completion of signal finding study, GNMX will have option to license development rights. At that point
    - GNMX will make upfront payment to Kirin in the "low single digit millions"
    - Kirin will choose of one two collaboration options
        - co-development/co-commercialization partnership. Under this scenario
            - GNMX will have U.S. and Canadian commercialization rights

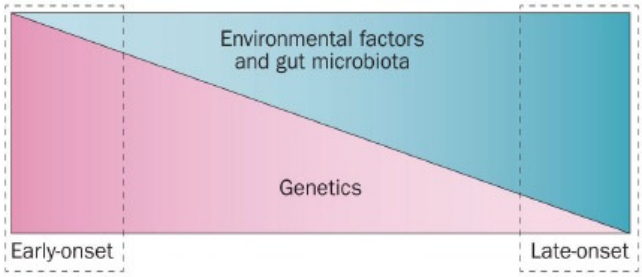
        - Kirin will have European and ROW (ex-U.S., ex-Canadian) commercialization rights
        - Sales and costs will be equally shared in the U.S. and Canada. GNMX receives double-digit royalty on sales outside of North America
    - licensing arrangement. Under this scenario
        - GNMX will have U.S., Canadian and European commercialization rights
        - Kirin will have ROW commercialization rights
        - GNMX funds development and retains 75% of profits in
- Specific terms of each of the two structures was not disclosed although GNMX notes that they "include a combination of royalties and profit sharing."

Severe Pediatric Onset Inflammatory Bowel Disease

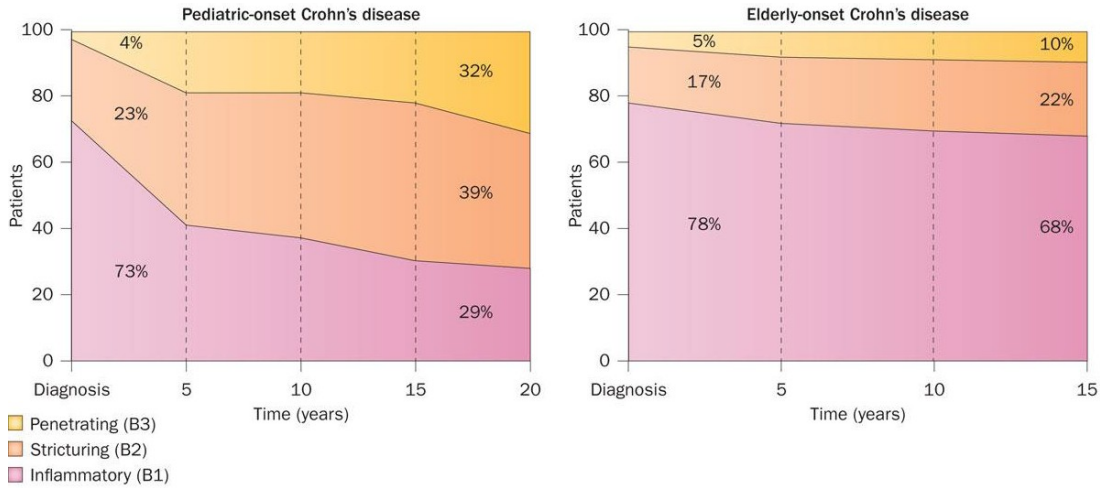
IBD is comprised of ulcerative colitis and Crohn's disease. U.S. prevalence of pediatric IBD is approximately 50k - 100k. Approximately 20% of IBD cases are initially diagnosed by adolescence. While similar in many respects, pediatric IBD has some unique characteristics as compared to the adult form. This includes a relationship between pediatric IBD and impaired growth and skeletal development. Genetics is also believed to play a much more significant role in the pediatric form of IBD. It is also typically more difficult to treat, less responsive to first-line treatments and often more severe than adult onset of the disease.

Ruel at el. found that genetics play a much more prominent role in pediatric, as opposed to adult-onset, IBD. In addition, over time pediatric Crohn's disease is much more likely to develop into more severe state and result in higher morbidity and mortality.

Genetics Much More Influential of Early Onset of IBD



SOURCE: Ruel, J. et al 2013

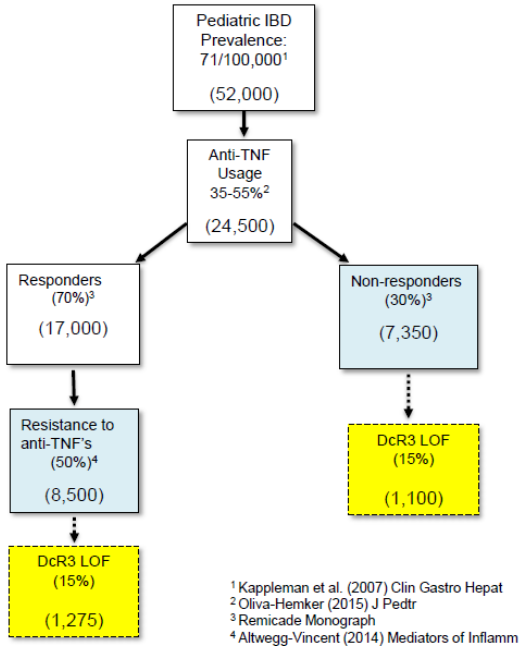


SOURCE: Ruel, J. et al 2013

Severe Pediatric Onset IBD is a chronic form of the disease, characterized by recurrent relapse of inflammation of the GI tract. Relapse can have serious consequences including chronic malnutrition, stunted growth and bowel resection surgery. Given the serious morbidity of pediatric IBD, relatively aggressive approaches to treating the disease have been employed.

While anti-TNFalpha therapy (infliximab) has been shown to induce and prolong IBD remission in children[1], it is ineffective in as many as 16k (~30%). And in those patients who do respond to anti-TNFalpha therapy, as many has one-half will develop resistance to it within 3 years. GNMX believes ~2k-3k of these individuals would be eligible for treatment with their anti-LIGHT monoclonal antibody.

Potential Anti-LIGHT Severe Pediatric IBD Patient Population



Anti-LIGHT monoclonal antibody

Research by Dr. Hakon Hakonarson, of CHOP's Center for Applied Genomics, and colleagues have identified decoy receptor 3 (DcR3), an immune regulatory protein as playing a role in Severe Pediatric Onset IBD.[2] In healthy individuals DcR3 binds to inflammatory proteins such as LIGHT (ligand for herpesvirus entry mediator). But in some individuals with IBD LIGHT are upregulated in the intestines, resulting in inflammation. Developing a direct substitute for DcR3 was found to not be feasible given its short half-life and toxicity.

The anti-LIGHT candidate, which is believed to mimic DcR3 regulation (i.e. downregulating inflammation) by binding to LIGHT, was discovered at La Jolla Institute for Allergy and Immunology and then licensed to Kirin which created a human version of the antibody. Sanofi then licensed it and, via a U.S. IND, brought it through phase I which showed that LIGHT is overexpressed in IBD. In 2015 Kirin regained rights.

The candidate 'fits' within the parameters of GNMX's collaboration with CHOP. It targets orphan populations, has been validated in phase I and has potential to rapidly move through development, has a moat of IP with 12 years of exclusivity in the U.S. and may have platform utility with possible follow-on orphan indications.

A single-center non-interventional study done by Sanofi demonstrated significantly higher levels of LIGHT in IBD patients versus healthy subjects, supporting the hypothesis that LIGHT plays a role in IBD.

GNMX development strategy will focus on patients with Severe Pediatric Onset IBD with DcR3 loss-of-function mutations and which have failed anti-TNF alpha therapy. The study will also enroll patients which do not have DcR3 loss-of-function mutations as controls.

[1] Dr. Carmen Cuffari. Diagnostic Considerations in Pediatric Inflammatory Bowel Disease Management. Gastroenterol Hepatol (N Y). 2009 Nov; 5(11): 775–783.
[2] Dr. Hakon Hakonarson, et al. Loci on 20q13 and 21q22 are associated with pediatric-onset inflammatory bowel disease. Nat Genet. 2008 Oct; 40(10): 1211–1215.

GNMX expects to complete a proof-of-concept study under the existing IND in the U.S. The company believes given the existing clinical trial supplies from Sanofi's study along with resources at CHOP that the POC study can be fairly fast-moving. Initial preparations towards initiating the study have been made including transfer of the clinical trial supplies and scheduled meetings with the joint development team (GNMX, Kirin, CAG). GNMX noted on the Q3 call that they made substantive progress with necessary preparations to begin the study including transferring the IND and a Type B meeting with the FDA. GNMX further noted that they are in the process of activating the IND and initiating the study. They continue to expect to have initial open-label responder data sometime in the first half of 2017.

If initial results are successful, GNMX believes there may be an opportunity to further expand to program to include all pediatric IBD anti-TNF alpha failures as well as move into other pediatric autoimmune diseases where DcR3 plays a role.

Development Path: Signal Finding Study Expected to Commence in Q4 2016
GNMX's proposed POC trial is a single-site (at CHOP), up to 12 patients study with 8 weeks of treatment using ascending doses. Clinical endpoints will be endoscopic evaluation (i.e. healing) and the Pediatric Crohn's Disease Index. The company estimates cost at approximately $2M. GNMX expects to have data from the proof-of-concept study in 1H 2017.

Based on the high unmet need and assuming positive results, GNMX would then hope to move directly to a single phase III pivotal trial (with orphan status). A long-term safety study will also be conducted.

Market Opportunity
Based on the 2k – 3k of Severe Pediatric Onset IBD patients that could be candidates for their anti-LIGHT therapy, including 1k+ non-responders to anti-TNF alpha therapy and 1k+ which initially respond but eventually build resistance to anti-TNF alpha therapy, and biologic pricing for ultra-orphan diseases, GNMX estimates this initial indication (i.e. Severe Pediatric Onset IBD) could be worth $300M - $400M. Any follow-on indications would offer additional upside

TARGT CNS
As a reminder the TARGT EPO program was recently shelved - at least for the time being. TARGT CNS program could have preclinical proof-of-concept data later in 2016

VALUATION: Value GNMX at $350M

We use an "average" orphan company valuation methodology based on statistics from the study done by Thomson Reuters Life Sciences Professional Services and Pfizer which we detailed in our June 2014 initiation report.

According to that study, the average per-year revenue of orphan drugs is approximately $600M. We have built a DCF model that more conservatively assumes $550M of revenue is generated over the remaining patent life of one orphan designated product. Other assumptions are that this product launches in 2020 (we think 2018 or 2019 launch is also reasonable), has 14 - 15 years of patent life remaining, revenue falls 50% per year each year after patent expiration and, given the high selling prices of orphan drugs, commands gross margins of 80% - 85%. We estimate operating expenses at just 20% of revenue given that orphan drugs can typically be detailed with a small sales force and relatively little overall marketing support. Using a 10% discount rate values the company at approximately $1.5B. Discounting this by the ~22% probability (per Thomson study) that an orphan drug in phase I eventually is approved, values the company at approximately $350M.

We continue to see fair value at approximately $350M or ~$10/share. Further successful progression through the development pathway should provide for additional de-risking and potential upside to our current $10/share target price.

APPENDIX: Refresher of Ongoing Development Programs

NFC-1

In September 2015 GNMX acquired neuroFix Therapeutics, LLC and its lead candidate NFC-1, a compound targeting CNS disorders associated with mutations of the metabotropic glutamate receptors (mGluRs). Initial focus is on Attention Deficit Hyperactivity Disorder (ADHD) and 22q11.2 Deletion Syndrome, a rare condition also associated with mGluR mutations and one which may offer orphan status opportunities (both specifically for 22q11.2 Deletion Syndrome as well as associated indications). This was the first opportunity to come from GNMX's relationship with CHOP

neuroFix was founded by Dr. Hakon Hakonarson, Director of the Center for Applied Genomics at CHOP, in order further develop NFC-1. Prior to GNMX's acquisition, neuroFix licensed certain technology related to ADHD and other neurological and neuropsychological indications from CHOP.

Terms of the deal;

- $8M in cash and common stock
- additional payments of up to $450M upon achievement of certain milestones (development, regulatory and sales) related to an oral formulation of NFC-1 and any new chemical entity (NCE) developed covering the same indication (specifics in terms of exactly what this relates to and what the triggers are were not disclosed)
- sales royalties based on tiered rates ranging from mid-to-high single digits depending on the product or NCE
- $25M for each FDA approved indication beyond the initial indication

Terms of License Agreement between neuroFix and CHOP;

- up to $1.5M in regulatory and sales milestones for each FDA approved indication using IP covering the agreement
- sales royalties based on a fluctuating rate in the low single digits - which adjust downward based on the extent of third party royalties
- $100k or less in annual maintenance fees
- a percentage (ranging from mid-single digits to mid-teens) of any sublicense income (ex-sublicensed sales by a certain party in Japan)
- this license agreement terminates upon the later of the expiration of certain CHOP patent rights and January 1, 2025, at which time neuroFix owns the covered licensed rights

Metabotropic Glutamate Receptors (mGluRs)

The amino acid glutamate is the most prominent excitatory neurotransmitter in the brain. It binds to mGluRs which are involved in the modulation of synaptic transmission and neuronal excitability in the central and peripheral nervous system. Genetic mutations of genes within the mGluR network have been associated with certain conditions including ADHD, anxiety disorders, schizophrenia and other neuropsychiatric disorders.

Research conducted by Dr. Hakonarson and colleagues indicated that mutations in the mGluR gene network are associated with a 10x higher rate of ADHD. They found that disruptions specifically to GRM1 (glutamate receptor, metabotropic 5), GRM3, GRM 7 and GRM8 were associated with ADHD.

NFC-1 GREAT Study

neuroFix, in collaboration with CHOP, conducted a phase 1, 30-patient, single arm study at Thomas Jefferson University (Philadelphia) assessing NFC-1 in adolescents with ADHD. Inclusion criteria included professionally diagnosed with ADHD and genotyped as having disruptions to the mGluR network. The background of the enrolled population had certain symptoms which could be considered particularly challenging to effectively treat including;

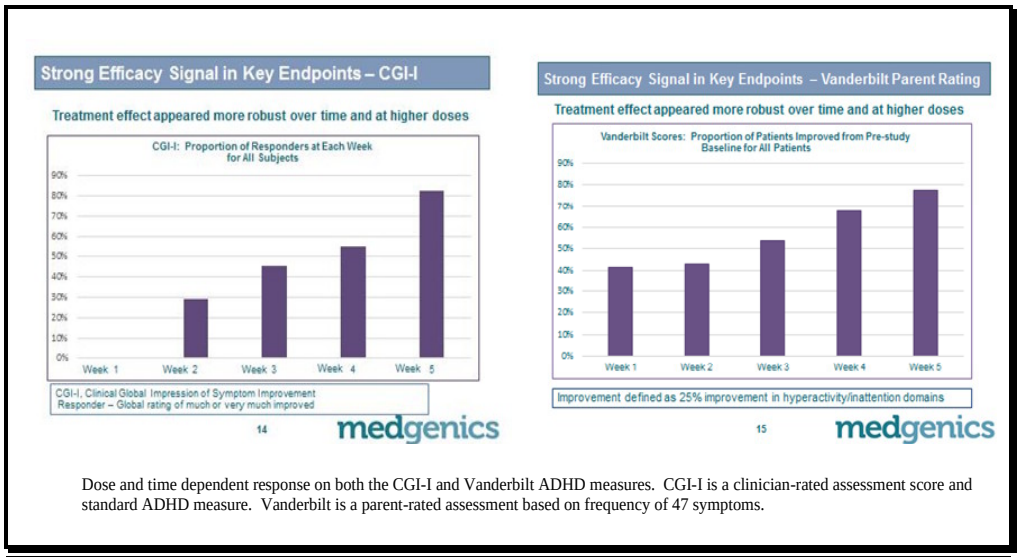
- 73% had severe ADHD (CGI-S>5, on a scale of 1=normal to 7=extremely ill)
- 67% had co-morbid psychiatric conditions such as anxiety, ODD and insomnia
- 30% were on antipsychotics and/or antidepressants
- 70% had been previously treated with ADHD drugs (with presumably little benefit)

One-week run-in on placebo was followed by four weeks of active treatment. Treatment was dose-escalating from 50mg (x2/day) to a maximum of 400mg (x2/day). Dose was escalated weekly. Patients were blinded,

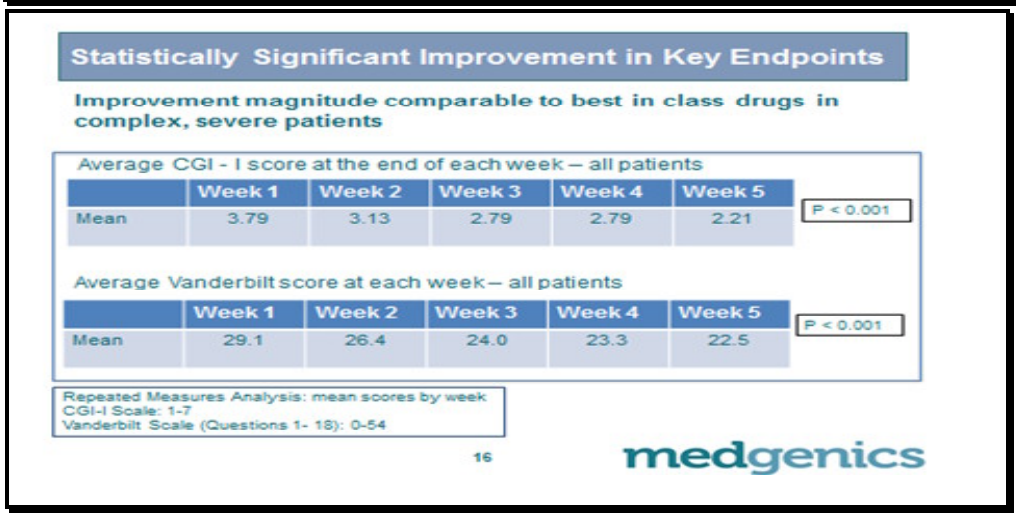
clinicians were not. Primary endpoint was safety, secondary endpoint efficacy measures were standard ADHD assessments including Vanderbilt and Clinical Global Impressions (CGI) scores.

Results showed;

- dose and time-dependent response on both the CGI-I and Vanderbilt measures
  - over 80% of patients responded to NFC-1 treatment on Vanderbilt measure at week 5
  - just under 80% of patients responded NFC-1 treatment on CGI-I measure at week 5
  - repeated measure analysis showed statistically significant response on both measures over time and at higher doses
- Mutations to "tier 1" genes (i.e those in the mGluR receptors) and "tier 2" genes (i.e. those that encode proteins that influence mGluR but are not in the receptors) showed much higher response rates compared to "tier 3" genes (more distant from the receptors and therefore likely to show lower response)
- Excellent safety with no treatment related serious adverse events
- 20 of the 30 patients chose to continue to receive NFC-1 therapy in an ongoing long-term safety trial. As management noted in their presentation, this is clearly a positive vote of confidence in the efficacy of NFC-1 given that there's a significant hassle involved in coming to the clinic on a regular basis to receive treatment (i.e. - it's unlikely patients/parents would continue if they experienced no positive effect)



Dose and time dependent response on both the CGI-I and Vanderbilt ADHD measures. CGI-I is a clinician-rated assessment score and standard ADHD measure. Vanderbilt is a parent-rated assessment based on frequency of 47 symptoms.



We note that there is the risk of unintended bias in the CGI-I score given that the clinician was not blinded in this study (management noted that the clinician is highly qualified in ADHD assessment, which we acknowledge is likely a mitigating factor). Risk of bias, however, is not relevant with Vanderbilt which is a parent-rated assessment as the parents were blinded in the study - and both CGI-I and Vanderbilt demonstrated dose and time dependent response, indicating that NFC-1 is effective in ADHD treatment. The recently initiated phase 2/3 will be double-blinded and therefore will not be at risk of bias.

Phase II/III Study SAGA (Study of Adolescent Glutamate Receptor Network Copy Number Variant ADHD) trial

Given the more pronounced response in tier 1 and tier 2 gene mutations, which are believed to account for 20% or more (GNMX's genotyping/phenotyping study showed prevalence of ~25%) of the ADHD population, this is an inclusion criteria in SAGA. SAGA is randomized, placebo-controlled study in adolescents (ages 12 – 17);

- enrollment (n=90), first patient enrolled in June
- will use same 23 trial sites as geno/pheno study
- randomize 1:1; NFC-1/placebo
- following wash-out period patients will
    - receive placebo or
    - receive NFC-1
        - in weekly escalating doses from 100mg (twice/day) to 400mg based on tolerability
        - after the 4th week patients will stay on the optimized dose for 2-week maintenance phase
        - followed by 1 week off-drug for safety observation
- Response endpoints will be ADHD RS (parent assessment) and Clinical Global Impressions (CGI-I)
    - as typical stimulant-based ADHD drugs are associated with significant side effects including anxiety and difficulty sleeping, this study will also assess sleep using adolescents sleep hygiene scale (ASHS) and anxiety with the screen for childhood anxiety related disorders (SCARED)

Management believes this study can also enroll rapidly, facilitated by the 95% of subjects in the pheno/geno study that indicated interest in continuing in future studies. GNMX expects top-line results to be available by the end of Q1 2017.

ADHD Market Is Attractive: *Positive Phase SAGA Data Could Be a Needle-Mover to Share Price*

ADHD could be a hugely attractive market for GNMX and a genetic-based therapy including the significant size of the market, ambiguity of diagnosis and unmet need for therapies which are more effective and have less problematic side effect profiles.

- ~6M children are diagnosed with ADHD in the U.S.
    - ~25% of ADHD population, or 1.5M, is mGluR+
    - based on pricing, dosing regimen and compliance of current ADHD drugs (~$12/day), this equates to a potential market opportunity for NFC-1 in ADHD of ~$3B – which could be conservative given that this assumes only 180 days/year of compliance and does not include the adult market
- ADHD is the most common neurobehavioral disorder diagnosed in the U.S.
- No definitive test exists to diagnose ADHD - all ADHD diagnoses are arbitrary based on subjective assessment
- Stimulants such as Adderrall (amphetamine and dextroamphetamine), Vyvanse (lisdexamfetamine) and ritalin (methylphenidate) account for over 90% of ADHD prescriptions. These drugs are associated with significant side effects including risk of addiction, irritability and difficulty sleeping, among others. They are highly regulated due to their risk of addiction. These stimulants do not always address all of the underlying symptoms which often can include anxiety and psychotic disorders - mGluR mutations have been associated with other psychiatric conditions which means NFC-1 may be able to address not only ADHD but other of these conditions as well

Unlike stimulants NFC-1 does address the underlying cause of ADHD. In addition, diagnosis (of mGluR mutations) is genetically-based, not arbitrary. It also (in clinical trials to-date, which includes a 1,000+ patient study in vascular dementia), has shown an excellent side-effect profile. And 20% - 25% of the entire U.S. ADHD market is very significant for a company of GNMX's size, particularly given that the benefits of NFC-1 over stimulants should offer the opportunity for premium pricing. We think it is conceivable that mGluR+ADHD could easily represent a multi-billion dollar market opportunity. As such, if the phase 2/3 study confirms what was demonstrated in phase 1, **we think this could be a needle-mover to the share price.**

22q11.2 Deletion Syndrome: *Orphan Opportunity for NFC-1 to Address Related Psychological Disorders*

22q11.2 Deletion Syndrome is a relatively rare disease with incidence (per *The International 22q11.2 Foundation Inc.*) estimated at one in every 1,000 live births - which equates to about 4,000 new cases every year in the U.S (~130k worldwide). We have not been able to find an estimate of prevalence rates, although management noted on the call that U.S. prevalence is believed to be approximately 75k - 100k.

22q11.2 Deletion Syndrome is characterized by the deletion on the long arm of one pair of chromosome 22 (region 1, band 1, sub-band 1). The disorder can affect most systems in the body and is associated with serious physical and neuropsychological problems including cardiovascular issues, cleft palate, abnormal facial features, immune disorders and behavioral, psychotic and anxiety disorders (including ADHD). And while many of the physical problems such as heart defects and cleft palate can be addressed by traditional medical intervention such as surgery, there are no current therapies available to address the psychological disorders. It is estimated that about 30% - 40% of individuals with 22q11.2 Deletion Syndrome will eventually progress to schizophrenia.

And mGluR mutations appear to play a roll in 22q11.2 Deletion Syndrome with over 90% of 22q11.2 Deletion Syndrome patients having at least one mGluR network related deletion. In fact two patients in the phase 1 ADHD study had 22q11.2 mutations (one deletion and one duplication), both of which, per the company's presentation, reported "significant symptom improvement in both CGI-I and Vanderbilt" and both patients continue in the long-term safety trial.

So GNMX will look to capitalize on the potential effect of NFC-1 in 22q11.2 Deletion Syndrome and in October initiated enrollment of a phase 1/2 indication and dose finding study. Open-label responder data is expected sometime during the first half of 2017. The initial study is expected to parse out the first (of potentially other follow-on) indication - which GNMX noted could be related to ADHD, anxiety or mood disorders.

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anti-LIGHT Severe Pediatric Onset Inflammatory Bowel Disease Program

In June 2016 GNMX announced that, in collaboration with Japanese biopharmaceutical company Kyowa Hakko Kirin, they initiated a development program with an anti-LIGHT monoclonal antibody for the ultra-orphan disease Severe Pediatric Onset Inflammatory Bowel Disease. This is the second program from the company's research collaboration with CHOP. It will leverage CHOP's Center for Applied Genomics (CAG), one of the world's largest repositories of pediatric genetic data.

Key points include;

- Phase 2-ready first-in-class biologic with available clinical supply
- GNMX will initiate signal finding study with Dr. Robert Baldassono, CHOP's Director for the Center of Pediatric IBD
- Kyowa Hakko Kirin has ~$3B in annual sales with focus on discovering antibody related drugs. Existing collaborations with large pharma include mogamulizumab (anti-CCR4) and benralizumab (anti-IL-5R alpha). Other collaborations include anti-FGF23a and anti-CD40 monoclonal antibodies
- Upon successful completion of signal finding study, GNMX will have option to license development rights At that point
    - GNMX will make upfront payment to Kirin in the "low single digit millions"
    - Kirin will choose of one two collaboration options
        - co-development/co-commercialization partnership. Under this scenario
            - GNMX will have U.S. and Canadian commercialization rights
            - Kirin will have European and ROW (ex-U.S., ex-Canadian) commercialization rights
            - Sales and costs will be equally shared in the U.S. and Canada. GNMX receives double-digit royalty on sales outside of North America
        - licensing arrangement. Under this scenario
            - GNMX will have U.S., Canadian and European commercialization rights
            - Kirin will have ROW commercialization rights
            - GNMX funds development and retains 75% of profits in
- Specific terms of each of the two structures was not disclosed although GNMX notes that they "include a combination of royalties and profit sharing.

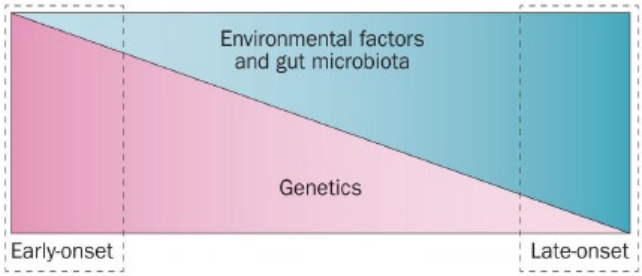
Severe Pediatric Onset Inflammatory Bowel Disease

IBD is comprised of ulcerative colitis and Crohn's disease. U.S. prevalence of pediatric IBD is approximately 50k - 100k. Approximately 20% of IBD cases are initially diagnosed by adolescence. While similar in many respects, pediatric IBD has some unique characteristics as compared to the adult form. This includes a relationship between pediatric IBD and impaired growth and skeletal development. Genetics is also believed to

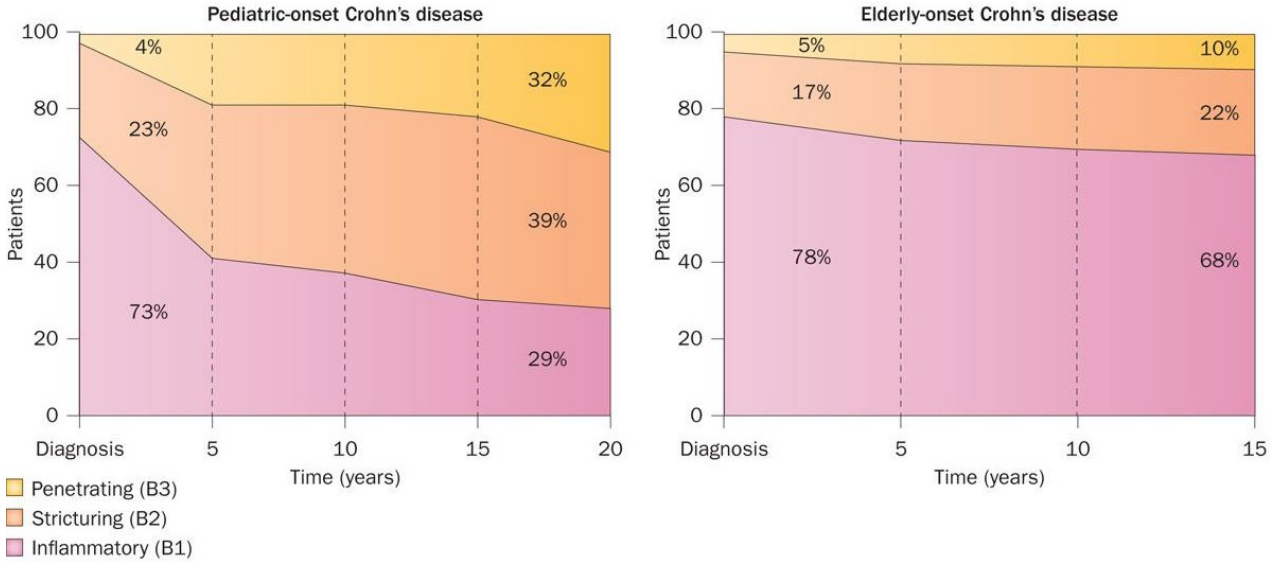
play a much more significant role in the pediatric form of IBD. It is also typically more difficult to treat, less responsive to first-line treatments and often more severe than adult onset of the disease.

Ruel at el. found that genetics play a much more prominent role in pediatric, as opposed to adult-onset, IBD. In addition, over time pediatric Crohn's disease is much more likely to develop into more severe state and result in higher morbidity and mortality.

Genetics Much More Influential of Early Onset of IBD



SOURCE: Ruel, J. et al 2013



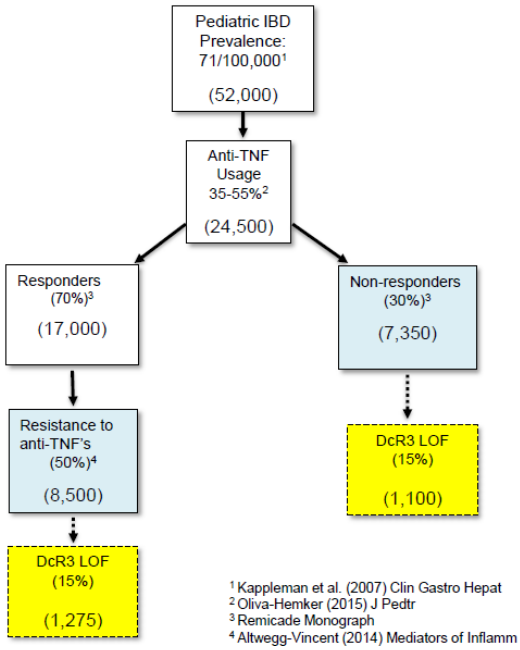
SOURCE: Ruel, J. et al 2013

Severe Pediatric Onset IBD is a chronic form of the disease, characterized by recurrent relapse of inflammation of the GI tract. Relapse can have serious consequences including chronic malnutrition, stunted growth and bowel resection surgery. Given the serious morbidity of pediatric IBD, relatively aggressive approaches to treating the disease have been employed.

While anti-TNFalpha therapy (infliximab) has been shown to induce and prolong IBD remission in children[3], it is ineffective in as many as 16k (~30%). And in those patients who do respond to anti-TNFalpha therapy, as many has one-half will develop resistance to it within 3 years. GNMX believes ~2k-3k of these individuals would be eligible for treatment with their anti-LIGHT monoclonal antibody.

[3] Dr. Carmen Cuffari. Diagnostic Considerations in Pediatric Inflammatory Bowel Disease Management. Gastroenterol Hepatol (N Y). 2009 Nov; 5(11): 775–783.

Potential Anti-LIGHT Severe Pediatric IBD Patient Population



Anti-LIGHT monoclonal antibody

Research by Dr. Hakon Hakonarson, of CHOP's Center for Applied Genomics, and colleagues have identified decoy receptor 3 (DcR3), an immune regulatory protein as playing a role in Severe Pediatric Onset IBD.[4] In healthy individuals DcR3 binds to inflammatory proteins such as LIGHT (ligand for herpesvirus entry mediator). But in some individuals with IBD LIGHT are upregulated in the intestines, resulting in inflammation. Developing a direct substitute for DcR3 was found to not be feasible given its short half-life and toxicity.

The anti-LIGHT candidate, which is believed to mimic DcR3 regulation (i.e. downregulating inflammation) by binding to LIGHT, was discovered at La Jolla Institute for Allergy and Immunology and then licensed to Kirin which created a human version of the antibody. Sanofi then licensed it and, via a U.S. IND, brought it through phase I which showed that LIGHT is overexpressed in IBD. In 2015 Kirin regained rights.

The candidate 'fits' within the parameters of GNMX's collaboration with CHOP. It targets orphan populations, has been validated in phase I and has potential to rapidly move through development, has a moat of IP with 12 years of exclusivity in the U.S. and may have platform utility with possible follow-on orphan indications.

A single-center non-interventional study done by Sanofi demonstrated significantly higher levels of LIGHT in IBD patients versus healthy subjects, supporting the hypothesis that LIGHT plays a role in IBD.

GNMX development strategy will focus on patients with Severe Pediatric Onset IBD with DcR3 loss-of-function mutations and which have failed anti-TNF alpha therapy. The study will also enroll patients which do not have DcR3 loss-of-function mutations as controls.

GNMX expects to complete a proof-of-concept study under the existing IND in the U.S. The company believes given the existing clinical trial supplies from Sanofi's study along with resources at CHOP that the POC study can be fairly fast-moving. Initial preparations towards initiating the study have been made including transfer of the clinical trial supplies and scheduled meetings with the joint development team (GNMX, Kirin, CAG). GNMX noted on the Q3 call that they made substantive progress with necessary preparations to begin the study including transferring the IND and a Type B meeting with the FDA. GNMX further noted that they are in the process of activating the IND and initiating the study. They continue to expect to have initial open-label responder data sometime in the first half of 2017.

[4] Dr. Hakon Hakonarson, et al. Loci on 20q13 and 21q22 are associated with pediatric-onset inflammatory bowel disease. Nat Genet. 2008 Oct; 40(10): 1211–1215.

If initial results are successful, GNMX believes there may be an opportunity to further expand to program to include all pediatric IBD anti-TNF alpha failures as well as move into other pediatric autoimmune diseases where DcR3 plays a role.

Development Path: Signal Finding Study Expected to Commence in Q4 2016
GNMX's proposed POC trial is a single-site (at CHOP), up to 12 patients study with 8 weeks of treatment using ascending doses. Clinical endpoints will be endoscopic evaluation (i.e. healing) and the Pediatric Crohn's Disease Index. The company estimates cost at approximately $2M. GNMX expects to have data from the proof-of-concept study in 1H 2017.

Based on the high unmet need and assuming positive results, GNMX would then hope to move directly to a single phase III pivotal trial (with orphan status). A long-term safety study will also be conducted.

Market Opportunity
Based on the 2k – 3k of Severe Pediatric Onset IBD patients that could be candidates for their anti-LIGHT therapy, including 1k+ non-responders to anti-TNF alpha therapy and 1k+ which initially respond but eventually build resistance to anti-TNF alpha therapy, and biologic pricing for ultra-orphan diseases, GNMX estimates this initial indication (i.e. Severe Pediatric Onset IBD) could be worth $300M - $400M. Any follow-on indications would offer additional upside

FINANCIAL MODEL

Aevi Genomic Medicine, Inc.

	2015 A	Q1A	Q2A	Q3A	Q4E	2016 E	2017 E	2018 E	2019 E
Total Revenues	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
YOY Growth	-	-	-	-	-	-	-	-	-
Cost of Goods Sold	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Gross Income	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Gross Margin	-	-	-	-	-	-	-	-	-
SG&A	$12,954.0	$4,191.0	$2,945.0	$3,042.0	$3,088.0	$13,266.0	$15,444.0	$15,925.0	$16,324.0
% SG&A	-	-	-	-	-	-	-	-	
R&D, net of grants	$23,614.0	$6,951.0	$8,741.0	$7,529.0	$8,521.0	$31,742.0	$32,444.0	$27,854.0	$26,824.0
% R&D	-	-	-	-	-	-	-	-	
Operating Income	($36,568.0)	($11,142.0)	($11,686.0)	($10,571.0)	($11,609.0)	($45,008.0)	($47,888.0)	($43,779.0)	($43,148.0)
Operating Margin	-	-	-	-	-	-	-		
Financial expense, net	($1,407.0)	($2.0)	($18.0)	$14.0	$8.0	$2.0	$0.0	$0.0	$0.0
Total Other Income (Expense)	($1,407.0)	($2.0)	($18.0)	$14.0	$8.0	$2.0	$0.0	$0.0	$0.0
Pre-Tax Income	($37,975.0)	($11,144.0)	($11,704.0)	($10,557.0)	($11,601.0)	($45,006.0)	($47,888.0)	($43,779.0)	($43,148.0)
Tax expense (benefit)	$17.0	$0.0	$3.0	$13.0	$0.0	$16.0	$0.0	$0.0	$0.0
Tax Rate	-	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*
Net Income	($37,992.0)	($11,144.0)	($11,707.0)	($10,570.0)	($11,601.0)	($45,022.0)	($47,888.0)	($43,779.0)	($43,148.0)
YOY Growth	*106.1%*	*-39.5%*	*31.2%*	*73.8%*	*-29.8%*	*18.5%*	*6.4%*	*-8.6%*	*-1.4%*
Net Margin	-	-	-	-	-	-	-	-	*#DIV/0!*
EPS	($1.51)	($0.34)	($0.35)	($0.29)	($0.31)	($1.28)	($1.17)	($1.02)	($0.94)
YOY Growth	*58.2%*	*-8.6%*	*16.0%*	*-148.8%*	*4.0%*	*-15.4%*	*-8.8%*	*-12.8%*	*-7.9%*
Diluted Shares O/S	25,078	32,954	33,470	37,081	37,085	35,147	41,000	43,000	46,000

Brian Marckx, CFA

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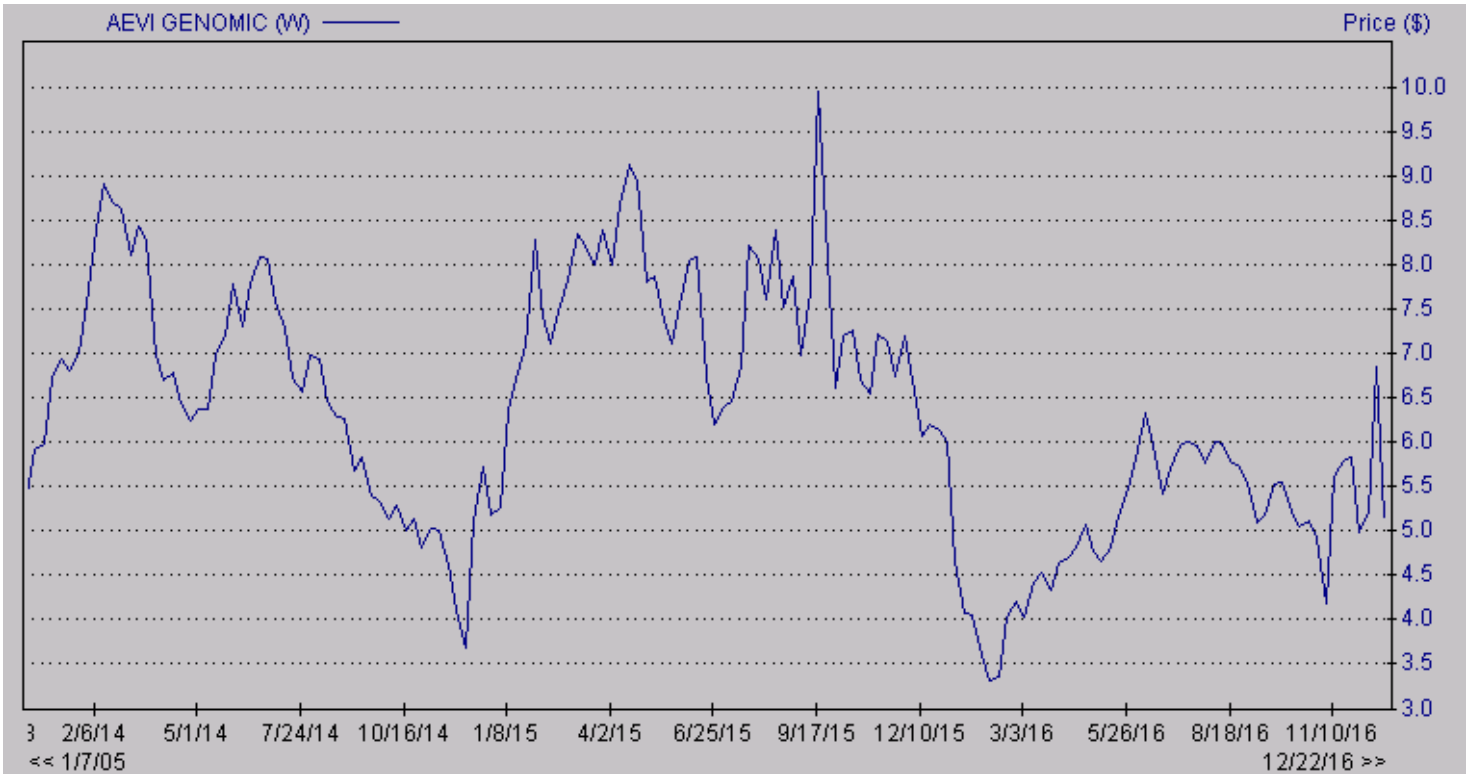

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