INITIATING COVERAGE
Biotechnology
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PTC THERAPEUTICS, INC. (NASDAQ:PTCT)

Initiation: Making Sense Out Of Nonsense

We are initiating coverage of PTC Therapeutics with an Outperform rating and a 12-month price target of $33. PTC combines the company's proprietary chemistry platforms with management's extensive expertise in gene expression modulation to develop orally available small molecules for rare genetic diseases.

Recommendation

Rating:	Outperform
Price Target (in $):	$33.00
Expected Return:	104.5%
Dividend:	NA
Enterprise Value (MM):	$514.2

Earnings Per Share

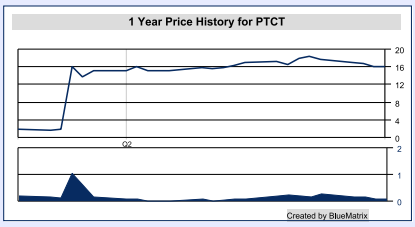
	2012A	2013E	2014E
Q1	--	*$(2.08)A*	*$(0.56)*
Q2	--	*$(0.77)*	*$(0.61)*
Q3	--	*$(0.44)*	*$(0.66)*
Q4	--	*$(0.06)*	*$(0.68)*
FY	$219.76	*$(2.88)*	*$(2.51)*
P/E	0.1x	NM	NM

Stock Statistics as of 07/25/2013 (in $)

Price:	$16.14
52W Range:	$18.50-$13.04
Shares Out (MM):	25.0
Market Cap (MM):	$402.4
Net Cash Per Share:	$7.36

Fundamentals

Revenue (MM) ('12A)	33.9
Revenue (MM) ('13E)	37.5
Revenue (MM) ('14E)	20.0



Lead Drug Candidate Ataluren: A Phase III Compound For Two Orphan Indications.

Ataluren suppresses nonsense mutations by inducing readthrough of premature stop codons. PTC has completed one Phase IIb clinical trial for nonsense mutation Duchene Muscular Dystrophy (nmDMD) and one Phase III clinical trial for nonsense mutation cystic fibrosis (nmCF), both of which demonstrated strong trends in clinical benefit. The company plans to seek conditional approval in the EU for both indications based on available clinical data. In the U.S., the ongoing Phase III clinical trial for nmDMD is expected to report top-line data in 1Q15 and PTC plans to initiate the Phase III clinical trial for nmCF in 2H13.

Ataluren Has Strong Clinical Potential For A Broad Range Of Indications.

Ataluren's mechanism of action applies to any genetic disorder that is caused by nonsense mutations, independent of the location of the affected gene. Preclinical studies conducted by both PTC and independent investigators have generated positive results supporting ataluren's activity in multiple inherited diseases caused by nonsense mutations, most of which are rare diseases that do not have any commercially available treatments. Therefore, PTC has strong upside potential by having the ability to target additional indications. Additionally, PTC has multiple technology platforms for modulating post transcriptional control. These platforms combined have the potential to address a multi-billion dollar market.

We Have Amended Our Initiation of Coverage Report Herein.

We have corrected an error in the P&L model that we published earlier this morning. This report contains our correct estimates for FY2013 EPS.

Please see addendum of this report for important disclosures.

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Investment Thesis

PTC Therapeutics is developing orally available small molecule compounds for the treatment of genetic disorders using the company's proprietary technologies that are based on post-transcriptional control processes. The company's lead drug candidate, ataluren, corrects nonsense mutations which present as premature stop codons, hence disallowing for biologically needed proteins. Ataluren is in Phase III clinical development for nonsense mutation Duchenne Muscular Dystrophy (nmDMD) and nonsense mutation cystic fibrosis (nmCF).

PTC has completed one Phase IIb clinical trial for nmDMD and one Phase III clinical trial for nmCF. Although both trials failed to achieve statistical significance in respective pre-specified primary endpoints, results from the two trials demonstrated promising trends of clinical benefit from treatment. A *post hoc* analysis of the nmDMD trial data demonstrated a trend towards statistical significance with the p value reaching 0.0561. Additionally, a subgroup analysis of the nmCF trial data demonstrated a much improved clinical benefit with the p value going from 0.0478 to 0.008. More importantly, PTC has identified the optimal patient populations for both indications and has designed the Phase III clinical trials accordingly to demonstrate maximum clinical benefit. Therefore, we are confident that both trials will deliver positive outcomes.

Ataluren is the only drug candidate currently in clinical development for nmDMD and nmCF patients. Our financial models, which are based on the nmDMD and the nmCF programs alone without a conditional approval in the EU for either program, suggests that ataluren can address a combined market of over $1 billion and that PTC shares are undervalued at the current level. Ataluren's activity in suppressing nonsense mutations can be applied to additional eligible genetic disorders and PTC has technology platforms that target other large unmet medical needs. Therefore, we believe there is significant upside potential and that PTC represents an attractive investment opportunity.

Exhibit 1. PTC Therapeutics, Inc. Company Snapshot

PTC is developing therapeutics for the treatment of rare genetic diseases through modulating post-transcriptional control. The company's lead candidate ataluren corrects nonsense mutations by inducing premature stop codon readthrough. PTC has completed a Phase IIb clinical trial in Duchenne Muscular Dystrophy and a Phase III clinical trial in cystic fibrosis. For both indications, the company plans to seek conditional approvals in the EU and to conduct Phase III clinical trials to support regulatory filings in the U.S.

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Senior Management	
Stuart W. Peltz, Ph.D.	CEO
Cláudia Hirawat	President
Shane Kovacs	CFO
Robert Spiegel, M.D.	CMO
Mark E. Boulding	EVP, Chief Legal Officer
Neil G. Almstead, Ph.D.	SVP, Research and CMC
John Babiial, Ph.D.	SVP, Drug Discovery Technologies
Jay Barth, M.D.	VP, Clinical Development

Capitalization	
Long-Term Debt (MM):	$0
Market Value of Equity (MM):	$384
Cash (MM):	$185
Technology Value (MM):	$200

Drug Candidate	Phase	Indication
Ataluren	Phase III	Duchenne Muscular Dystrophy
	Phase III	Cystic fibrosis
TBD	Preclinical	SMA
PTC596	Preclinical	Chemo-resistant cancers

Source: Cowen and Company

One Candidate For Two, And Potentially Many More, Orphan Indications

PTC's lead drug candidate, ataluren, is targeting two Orphan indications: Duchenne Muscular Dystrophy (DMD) and cystic fibrosis (CF). DMD affects approximately one in every 3,500 new born children, specifically boys. This translates into approximately 14,000 DMD patients in the U.S. The prevalence of CF is approximately 30,000 in the U.S. and approximately 70,000 worldwide. The lack of treatment and the devastating nature of both indications have created a significant unmet medical need. In approximately 13% of the DMD patient population and approximately 10% of the CF patient population, the diseases are caused by nonsense mutations that can potentially be corrected with ataluren treatment, which induces readthrough of premature stop codons during protein translation. Our revenue buildup model suggests that ataluren's target population includes approximately 1,500 DMD patients and 3,000 CF patients in the U.S. alone.

Ataluren has been granted Orphan Drug Status for the treatment of nonsense mutation DMD (nmDMD) and nonsense mutation CF (nmCF) by the FDA and has been designated an Orphan Medical Product by the EMA. Additionally, ataluren has received Fast Track Designation for the treatment of nmDMD in the U.S.

Based on its mechanism of action, ataluren can be used for the treatment of not only nmDMD and nmCF but any genetic disorder that is caused by nonsense mutations. Studies conducted by PTC and other independent investigators suggest that ataluren promotes readthrough of nonsense mutations in multiple rare genetic disorders independent of the affected gene and the location of the disease-causing genetic mutation. PTC has successfully completed multiple Phase I clinical trials to establish the safety and tolerability of ataluren in humans and has also identified the optimal dosing regimen through Phase II dose finding studies. Although we believe that it is in the best interest of PTC to first focus on achieving regulatory approval and commercializing ataluren for nmDMD and nmCF, should the company make the strategic decision to pursue additional indications with ataluren, the available clinical data should help PTC complete the clinical development process at a relatively faster pace. Therefore, both ataluren and consequently PTC have significant upside potential, in our opinion.

PTC has retained worldwide commercialization rights to ataluren for all indications. A focus on Orphan indications has created a lower hurdle for PTC to pursue independent commercialization thereby maximizing the upside profit potential once ataluren receives regulatory approval.

Conditional Approval In The EU: Upside Potential

PTC has completed one Phase IIb clinical trial for nmDMD and one Phase III clinical trial for nmCF. Although neither trial achieved statistical significance in the pre-specified primary endpoint analyses, data from both trials demonstrated highly promising trends. Moreover, statistically significant clinical benefit with ataluren treatment was achieved in the *post hoc* analysis of the nmDMD trial data and subgroup analysis of the nmCF trial data.

PTC submitted an application to the European Medicines Agency (EMA) in October 2012 seeking conditional approval of ataluren for the treatment of nmDMD based on the data from the Phase IIb clinical trial. In the initial response that the EMA sent to the company in March 2013, the agency raised a few major objections that if "not adequately addressed", would preclude a recommendation for marketing authorization for ataluren, which included "insufficient efficacy" from the completed single Phase IIb clinical trial and "uncertainties about the right dose of the drug". PTC expects to submit responses to the day 120 list of questions in July 2013 and stated that the company has reasonable responses to all of the major objections.

Additionally, PTC expects to submit an application for conditional approval for nmCF in 2H13 based on the results from the completed Phase III clinical trial. We are taking a conservative approach by not including a conditional approval for either nmDMD or nmCF in our revenue buildup model and company valuation. However, we believe that a real possibility does exist that the EMA may find PTC's responses to the questions on nmDMD acceptable and/or find the data from the nmCF trials to be strong enough to support a positive risk-to-benefit balance and hence grant conditional approval(s) to PTC.

Information From Previous Trials Will Help In Confirmatory Trial Designs

Should ataluren receive conditional approval for nmDMD in the EU, the ongoing Phase III clinical trial will become a post-approval confirmatory study for the EU and will be a registration study in the U.S. In the case of no conditional approval in the EU, PTC plans to conduct the study as a registration study for both territories. The same scenario applies to nmCF as well. For the ease of description, we use the term "confirmatory Phase III clinical trial" for both studies in this report. Based on the information obtained from the completed trials, PTC has modified the design of the confirmatory Phase III clinical trial for nmDMD and is also finalizing the design of the confirmatory study for nmCF.

PTC has designed the confirmatory Phase III clinical trial for nmDMD to enroll patients who are in the declining phase of their muscle function so that the clinical benefit of ataluren treatment as compared to placebo can be best demonstrated. A subgroup analysis of the Phase IIb clinical trial data in patients who would qualify for the Phase III clinical trial reached statistical significance (p=0.0096). The confirmatory Phase III clinical trial is ongoing and top-line data are expected in 1H15.

Similarly, PTC plans to enroll nmCF patients who are not taking inhaled tobramycin (TOBI) in the confirmatory Phase III clinical trial since a subgroup analysis of the completed Phase III clinical trial data suggests that the use of TOBI interferes with the mechanism of action of ataluren. The trial will be initiated in 2H13. We believe that PTC has identified the optimal patient population for both confirmatory Phase III clinical trials to demonstrate maximum clinical benefit.

Exhibit 2. PTC Therapeutics, Inc. Upcoming Milestones

	Events	Time
nmDMD	Submission of reponse to the day 120 list of questions to the EMA	Jul-13
	Potential conditional approval in the EU	2H13
	Completion of patient enrollment for the confirmatory Phase III clinical trial	Mid-2014
	Top-line data from the confirmatory Phase III clinical trial	Mid-2015
	FDA and MAA filing for full approval	2H15
nmCF	MAA filing for conditional approval in the EU	2H13
	Initiation of confirmatory Phase III clinical trial	1H14
	Potential conditional approval in the EU	2H14
	Completion of patient enrollment for the confirmatory Phase III clinical trial	2H15

Source: PTC Therapeutics, Inc. & Cowen and Company

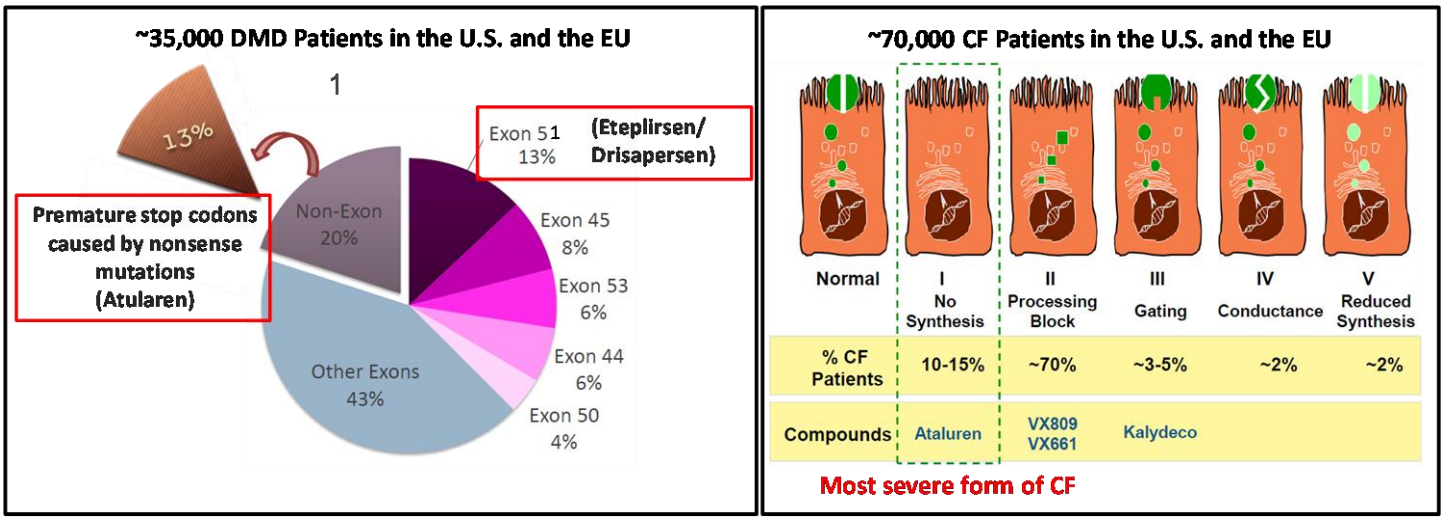
As the above table indicates, there are an abundance of upcoming milestones for PTC. We expect PTC's future stock performance will be fueled by the upcoming news flow, and therefore we believe that now is the time to invest in the stock.

Competition Is Limited To Non-Existent

PTC's ataluren targets the sub-populations of DMD and CF patients whose diseases are caused by nonsense mutations in the genes. Approximately 13% of DMD patients have this type of mutation and there is no overlap between nonsense mutation patients and the patients with diseases caused by deletion mutations. The clinical development activities in the DMD space have received significant attention not only because of the huge unmet medical need and the substantial market potential, but also because of the head-to-head competition between two companies, Sarepta Therapeutics (SRPT, Outperform) and Prosensa (partnered with GSK), both of which are developing exon-skipping technology-based therapeutics for the deletion mutation in DMD patients. However, the competition between these two companies will have no impact on PTC as their technologies target mutually exclusive patient populations.

Similarly in CF, there are multiple types of mutations that are responsible for the disease and ataluren is the only drug candidate currently in clinical development for nonsense mutations. Two other main classes of mutations in the *CFTR* gene cause a defect in CFTR protein trafficking (which prevents the protein, a chloride ion channel, from reaching the cell membrane) and ion channel gating (which prevents the chloride ion channel on the cell membrane from opening and closing properly). Kalydeco was the first FDA-approved medication to address the underlying cause of CF and targets the ion channel gating mutations. Vertex Pharmaceuticals, which developed and is commercializing Kalydeco, has follow-on programs for CF but none are targeting nonsense mutation patients.

Exhibit 3. Ataluren Targets Distinct Sub-Populations Of Both DMD And CF Patients



Source: PTC Therapeutics, Inc., Sarepta Therapeutics, Inc, & Cowen and Company

Combining Partnerships And Proprietary Programs For A Deep And Robust Pipeline

PTC owns the worldwide rights to ataluren, which was developed using the company's proprietary platform technology. Given the limited patient populations of Orphan indications, we believe that the company will be able to commercialize ataluren independently in both the U.S. and the EU upon regulatory approval should management make the strategic decision to pursue this path.

PTC has also entered into collaborative agreements with Roche and the Spinal Muscular Atrophy Foundation to develop a preclinical drug for SMA, a rare inherited central nervous system disease. PTC received an upfront payment of $30 million from Roche as part of the collaboration agreement and the company could receive an additional $460 million if various milestones are achieved.

PTC has complete control over additional multiple early-stage programs that target both Orphan indications and diseases that affect large patient populations. PTC will have the flexibility to either pursue independent clinical development of the programs or enter into partnerships to help defray development costs.

Exhibit 4. PTC Has A Robust Pipeline

Program/Target	Indication	Stage of Development	Commercial Rights
Genetic Disorders			
Ataluren	nmDMD	MAA for conditional approval submitted: Oct 2012 Confirmatory Phase III ongoing	PTC
Ataluren	nmCF	MAA for conditional approval target: 2H13 Confirmatory Phase III planned: 2H13	PTC
SMN2	SMA	Lead development compound selection in 2H13	Roche
Utrophin	DMD	Lead optimization	PTC
Serca2a	DMD	Lead optimization	PTC
Oncology			
PTC596 (BMI1)	Chemo-resistant cancers	IND ready	PTC
Infectious Diseases			
PTC725 (NS4b)	HCV	IND ready	PTC
Antibacterial	MDR Gram-negative bacteria	Lead development compound selection in 2H13	PTC
Virology	HIV latency, Dengue	Discovery / optimization	PTC

Source: PTC Therapeutics, Inc.

Management's Expertise Is A Valuable Asset

Stuart Peltz, Ph.D. is a co-founder of the company and has served as CEO as well as a member of the Board of Directors since the company's inception in 1998. A long-time professor of molecular genetics, Dr. Peltz's research in academia focused on understanding the mechanism of post-transcriptional control processes and he is an elected fellow of The American Association for the Advancement of Science (AAAS), an international scientific society founded in 1848. This extensive academic expertise is the foundation of PTC's technology platforms.

Additionally, Dr. Peltz is widely regarded as the one of the pioneers in characterizing the natural history of DMD and his publications on this topic have been heavily cited by other research groups. We believe PTC's clinical development activities, particularly those in nmDMD, including trial design and data analysis and interpretation, will benefit significantly from management's deep knowledge of the diseases being targeted.

A Strong Balance Sheet Provides Solid Support For Vigorous Clinical Development

In June 2013, PTC successfully completed an Initial Public Offering (IPO), raising a total of approximately $134 million in net proceeds. The IPO followed on the heels of a final round of private financing that was completed in March 2013 and brought in $65 million. We believe the strong balance sheet will be sufficient for the company to complete the confirmatory Phase III clinical trial for ataluren in nmDMD, which we believe is the most important milestone for PTC. Additionally, PTC is entitled to payments from Roche if certain milestones are achieved.

Significant Market Potential Creates An Attractive Investment Opportunity

We have employed multiple valuation matrices to our modeled assumptions, which all suggest that PTC shares are undervalued at current levels. We take a conservative approach to valuation by not including EU conditional approval for either nmDMD or nmCF in our revenue projections. Additionally, we are estimating rather conservative penetration rates for ataluren in both nmDMD and nmCF, even though there are no other therapeutics currently under clinical development for these distinct patient populations. We estimate that ataluren, if approved, will be able to command a price that is comparable to Kalydeco, the small molecule drug from Vertex for the treatment of CF in patients where the disease is caused by a gating mutation in the gene. Our revenue buildup model suggests that ataluren has a market potential of approximately $1 billion by targeting the nmDMD and nmCF indications alone.

Exhibit 5. Ataluren Has Significant Market Potential

	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E
Ataluren for Duchenne Muscular Dystrophy (DMD)										
U.S.										
Number of diagnosed DMD patients in the U.S.	11,429	11,880	12,321	12,753	13,174	13,586	13,988	14,380	14,764	15,138
% of DMD patients with nonsense mutations	*13.0%*	*13.0%*	*13.0%*	*13.0%*	*13.0%*	*13.0%*	*13.0%*	*13.0%*	*13.0%*	*13.0%*
Number of U.S. DMD patients amenable to treatment with ataluren	1,486	1,544	1,602	1,658	1,713	1,766	1,818	1,869	1,919	1,968
% Market penetration by ataluren	*10.0%*	*30.0%*	*40.0%*	*50.0%*	*55.0%*	*60.0%*	*65.0%*	*70.0%*	*70.0%*	*65.0%*
Number of U.S. DMD patients receiving ataluren treatment	149	463	641	829	942	1,060	1,182	1,309	1,344	1,279
AWP	$125,000	$250,000	$250,000	$250,000	$250,000	$250,000	$250,000	$250,000	$250,000	$250,000
U.S. total ataluren revenue from DMD ($MM)	**18.6**	**115.8**	**160.2**	**207.2**	**235.5**	**264.9**	**295.5**	**327.2**	**335.9**	**319.8**
EU										
Number of dianosed DMD patients in EU	15,009	15,634	16,250	16,854	17,448	18,031	18,604	19,167	19,720	20,263
% of DMD patients with nonsense mutations	*13.0%*	*13.0%*	*13.0%*	*13.0%*	*13.0%*	*13.0%*	*13.0%*	*13.0%*	*13.0%*	*13.0%*
Number of EU DMD Patients eligible for ataluren treatment	1,951	2,032	2,112	2,191	2,268	2,344	2,419	2,492	2,564	2,634
% Market penetration by ataluren	*5.0%*	*20.0%*	*25.0%*	*30.0%*	*35.0%*	*40.0%*	*45.0%*	*50.0%*	*55.0%*	*55.0%*
Number of EU DMD patients receiving ataluren treatment	98	406	528	657	794	938	1,088	1,246	1,410	1,449
AWP	$87,500	$175,000	$175,000	$175,000	$175,000	$175,000	$175,000	$175,000	$175,000	$175,000
EU total ataluren revenue ($MM)	**8.5**	**71.1**	**92.4**	**115.0**	**138.9**	**164.1**	**190.5**	**218.0**	**246.7**	**253.5**
WW total ataluren DMD revenue ($MM)	**27.1**	**187.0**	**252.6**	**322.3**	**374.4**	**429.0**	**486.0**	**545.2**	**582.6**	**573.3**
Ataluren for cystic fibrosis (CF)										
U.S.										
U.S. prevalence of CF		33,295	33,794	34,301	34,816	35,338	35,868	36,406	36,952	37,507
% of CF patients with nonsense mutations		*10.0%*	*10.0%*	*10.0%*	*10.0%*	*10.0%*	*10.0%*	*10.0%*	*10.0%*	*10.0%*
Number of U.S. nmCF patients		3,330	3,379	3,430	3,482	3,534	3,587	3,641	3,695	3,751
% of nmCF patients who can discontinue TOBI		*50.0%*	*50.0%*	*50.0%*	*50.0%*	*50.0%*	*50.0%*	*50.0%*	*50.0%*	*50.0%*
Number of U.S. CF patients amenable to treatment with ataluren		1,665	1,690	1,715	1,741	1,767	1,793	1,820	1,848	1,875
% Market penetration by ataluren		*5.0%*	*15.0%*	*25.0%*	*30.0%*	*35.0%*	*40.0%*	*45.0%*	*50.0%*	*50.0%*
Number of U.S. CF patients receiving ataluren treatment		83	253	429	522	618	717	819	924	938
AWP		$125,000	$250,000	$250,000	$250,000	$250,000	$250,000	$250,000	$250,000	$250,000
U.S. total ataluren revenue from CF ($MM)		**10.4**	**63.4**	**107.2**	**130.6**	**154.6**	**179.3**	**204.8**	**231.0**	**234.4**
EU										
EU prevalence of CF		44,175	44,617	45,063	45,514	45,969	46,428	46,893	47,362	47,835
% of CF patients with nonsense mutations		*10.0%*	*10.0%*	*10.0%*	*10.0%*	*10.0%*	*10.0%*	*10.0%*	*10.0%*	*10.0%*
Number of U.S. nmCF patients		4,418	4,462	4,506	4,551	4,597	4,643	4,689	4,736	4,784
% of nmCF patients who can discontinue TOBI		*50.0%*	*50.0%*	*50.0%*	*50.0%*	*50.0%*	*50.0%*	*50.0%*	*50.0%*	*50.0%*
Number of EU CF patients amenable to treatment with ataluren		2,209	2,231	2,253	2,276	2,298	2,321	2,345	2,368	2,392
% Market penetration by ataluren		*2.5%*	*10.0%*	*20.0%*	*25.0%*	*30.0%*	*35.0%*	*40.0%*	*40.0%*	*40.0%*
Number of U.S. CF patients receiving ataluren treatment		55	223	451	569	690	812	938	947	957
AWP		$87,500	$175,000	$175,000	$175,000	$175,000	$175,000	$175,000	$175,000	$175,000
EU total ataluren revenue from CF ($MM)		**4.8**	**39.0**	**78.9**	**99.6**	**120.7**	**142.2**	**164.1**	**165.8**	**167.4**
WW total ataluren CF revenue ($MM)		**15.2**	**102.4**	**186.1**	**230.1**	**275.3**	**321.5**	**368.9**	**396.7**	**401.8**
WW total ataluren sales revenues to PTC ($MM)	**27.1**	**202.2**	**355.0**	**508.3**	**604.5**	**704.3**	**807.5**	**914.1**	**979.3**	**975.2**

Source: Cowen and Company

Ataluren Makes Sense Of The Nonsense Mutations

Ataluren is an orally available small molecule that corrects genetic nonsense mutations in patients to help produce a functional protein that is otherwise missing in these patients.

Nonsense Mutations Create Premature Stop Codons

Nonsense mutations are point mutations in DNA that result in the creation of premature stop codons – UAA, UAG or UGA within the coding regions of messenger RNA (mRNA). Normal stop codons at the end of mRNA complete protein translation. In contrast, premature stop codons, which can be located anywhere between the start codon that initiates protein translation and the normal stop codon, terminate protein translation before the translation machinery reaches the end of the mRNA. As a result, the produced protein is truncated and often lacks proper structure and functionality. Moreover, mRNAs containing premature stop codons are susceptible to nonsense-mediated mRNA decay (NMD), a cellular surveillance pathway that functions to reduce gene expression errors. In reality, the NMD pathway efficiently recognizes and degrades the vast majority of transcripts generated from nonsense mutations. Therefore, nonsense mutations often lead to complete elimination of protein production.

Approximately 11% of all described human genetic disorders are caused by nonsense mutations. In addition to Duchenne Muscular Dystrophy (DMD) and cystic fibrosis (CF), additional indications that can potentially be addressed by ataluren include:

- Miyoshi Myopathy: an autosomal recessive muscular dystrophy that can be caused by nonsense mutations in the *dysferlin* gene
- Beta Thalassemia: an inherited blood disorder caused by the loss of hemoglobin production
- Hurler Syndrome: the most severe form of lysosomal storage disorder mucopolysaccharidosis 1, caused by the loss of the enzyme alpha-L-iduronidase
- Usher Syndrome: the most common form of congenital deaf-blindness in humans and the most severe subtype is caused by nonsense mutations in the *USH1C* gene
- Familial Pulmonary Arterial Hypertension (FPAH): an indication that can be due to nonsense mutations in the *BMPR2* gene, the *SMAD8* gene or the *SMAD9* gene
- Carnitine Palmitoyltransferase 1A (CPT1A) Deficiency: a metabolic disorder caused by mutations in the *CPT1A* gene; and
- additional rare genetic disorders and certain types of cancers

Overall, an estimated 2.5 million patients have nonsense mutation-related genetic disorders In the U.S. Therefore, ataluren has a significant addressable market, which has the potential to provide PTC with substantial upside.

Promoting Premature Stop Codon Readthrough: The Aminoglycosides' Other Life

Aminoglycosides, a class of antibiotics used mainly for the treatment of Gram-negative bacterial infections, have been known for their activity in promoting readthrough of premature stop codons. The first discoveries were reported in the 1960's when the addition of aminoglycosides suppressed nonsense mutations in both *E. coli* and budding yeast *Saccharomyces cerevisiae*. Similar suppression was later confirmed in mammalian cell,s which spurned clinical trials to evaluate aminoglycosides in treating genetic disorders caused by nonsense mutations.

Genetic and biochemical studies have suggested that the reason for the nonsense mutation suppression by aminoglycosides is due to the reduced fidelity in protein synthesis. The high fidelity during translation from messenger RNA (mRNA) to protein relies on complementary Watson-Crick base-pair matching. The ribosome uses mRNA as a template and aminoacyl-tRNA (aa-tRNA, transfer RNA (tRNA) molecules that are bound to amino acids) as substrates to synthesize polypeptide chains. Based on the correct base matching between the genetic codons contained in the mRNA and the anticodons in the aa-tRNAs, the ribosome recognizes cognate (complete match) and rejects non-cognate or near-cognate aa-tRNA. Non-cognate aa-tRNAs generally have two or three mismatches within one genetic codon, which consists of three nucleotides, and near-cognate aa-tRNA usually contain one mismatch. Near-cognate aa-tRNA is much more likely to be incorporated by error during protein synthesis and discrimination against near-cognate aa-tRNA is partly based on the structure of the ribosomes and their recognition of the geometry of codon-anticodon base pairing.

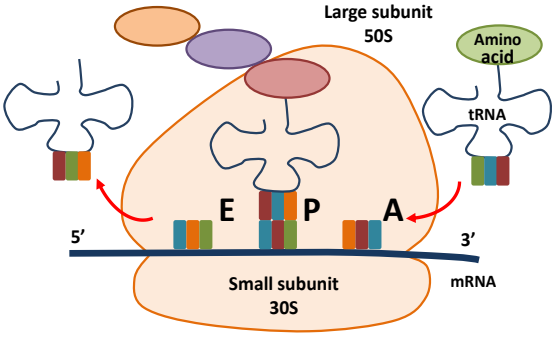
The "proofreading" mechanism of the ribosome ensures that genetic information is accurately translated from DNA to protein by preventing unmatched aa-tRNAs from becoming incorporated into the polypeptide chain.

A ribosome has three sites:

- The A site (aminoacyl-tRNA site) where new tRNA molecules that are bound to amino acids enter the ribosome
- The P site (peptidyl-tRNA site) in the middle which is the next stop for tRNA molecules after the A site during peptide elongation; and
- The E site (the exit site) where both the tRNA molecules that have detached from the amino acids and the newly synthesized polypeptide chain leave the ribosome.

Protein synthesis begins when an mRNA template containing the start codon AUG is recognized by the ribosome and the assembly of the translation initiation complex is complete. Termination of protein synthesis occurs when one of the three stop codons, UGA, UAG, or UAA, occupies the A site. The stop codons are recognized not by any tRNAs but instead by proteins called release factors, which terminate protein biosynthesis and release the nascent polypeptide chain from the ribosome.

Exhibit 6. Protein Synthesis At The Ribosome



Source: Cowen and Company; Adapted from Molecular Biology of the Cell (Published by Garland Science)

Two additional sites within a ribosome, T (elongation factor Tu) site and I (initiation) site, are located next to A site and are active during mRNA decoding or during the initiation of protein synthesis. Aminoglycosides, by binding to the decoding sites in the ribosomes, induce a conformational change that reduces near-cognate aa-tRNA discrimination. As a result, a near-cognate aa-tRNA is able to compete with the release factors to insert an amino acid where the premature stop codon is positioned and the mis-incorporation allows protein translation to skip the premature stop codon to reach the natural stop codon, leading to the production of the full length protein.

Preclinical And Clinical Studies Of Aminoglycosides Have Generated Positive Data ...

Aminoglycosides have been assessed for the treatment of genetic disorders caused by nonsense mutations in both preclinical and clinical studies. The proof-of-concept studies evaluating the concept of utilizing aminoglycoside-induced nonsense mutation suppression in treating genetic disorders was first conducted in the nmCF disease model. Mammalian cells that contain nonsense mutations in the *CFTR* gene were treated with two different types of aminoglycosides: G-418 (Geneticin) and gentamicin. Expression of full-length CFTR protein and restoration of cyclic AMP (cAMP)-activated chloride channel activity were observed in the cells after treatment.

In a nmCF mouse model that carries a nonsense mutation containing the human *CFTR* gene, production of the full-length CFTR protein was observed following treatment with gentamicin, tobramycin or amikacin. Measurement of cAMP-activated chloride channel conductance

confirmed the functional improvement of the newly produced CFTR protein. In human studies, both the topical application to the nose of gentamicin drops and intravenous administration of gentamicin have demonstrated improvement in chloride ion transport in nasal epithelial cells.

Similarly in nmDMD mouse models where muscular dystrophy is caused by nonsense mutations in the *dystrophin* gene, gentamicin has been shown to increase the production of full-length dystrophin protein that was correctly localized and improved disease symptoms. The effects have been replicated in human patients carrying nonsense mutations in the *dystrophin* gene in clinical trials. In a study conducted by Malik et al., at the Nationwide Children's Hospital which evaluated the short-term and long-term administration of gentamicin in nmDMD patients, 14-day treatment with intravenous gentamicin reduced serum creatine kinase (CK) by 50%. Furthermore, six months of gentamicin treatment significantly increased dystrophin protein levels ($p=0.027$), with the highest levels reaching approximately 15% of normal, resulting in the improvement in clinical outcome measurements as well. Importantly, gentamicin's specificity for premature stop codon readthrough was validated since no treatment effects were detected in eight DMD patients who were carrying frame-shift mutations in their *dystrophin* genes.

Aminoglycosides have demonstrated promising results in nonsense mutation suppression in several other genetic disease models such as Hurler's syndrome, nephropathic cystinosis, late infantile neuronal ceroid lipofuscinosis and oncology disorders involving the *p53* gene in addition to nmDMD and nmCF.

… However, Toxicity Is Concerning

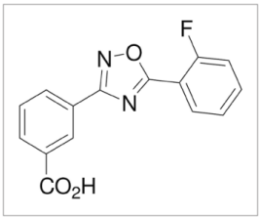
Aminoglycosides are far from an ideal therapeutic for these genetic disorders due to severe nephrotoxicity and ototoxicity associated with the long-term administration of aminoglycosides even at relatively low serum concentrations. In many cases, the toxicity is irreversible and the resulting damage to patients can be permanent. Development of resistance and the need for intravenous infusion are additional hurdles for chronic use of aminoglycosides. Moreover, this family of antibiotics has demonstrated only modest efficacy in inducing full-length protein production. Therefore, an orally available small molecule that is safer and more potent is highly desirable, hence the discovery and need for ataluren.

Ataluren: Higher Potency And Better Safety

Ataluren was discovered by PTC in house using the company's proprietary technology platform involving an extensive screening process. PTC conducted two high-throughput screens from a total of 800,000 low molecular weight compounds to identify candidates that promoted readthrough of the premature stop codon UGA. The first screen was conducted in human embryonic kidney cells (HEK293) stably expressing a luciferase reporter gene in which a nonsense mutation had been introduced to create a premature stop codon, UGA. The second screen was conducted in a cell-free translation system with synthetic luciferase mRNA that contained a nonsense mutation.

Compounds that demonstrated readthrough activity but minimal toxicity on the cells were further characterized for their potency and activity, including the dose-response relationship and the readthrough activity on the other two premature stop codons UAA and UAG. Several classes of chemical scaffolds were identified from the process for chemical lead optimization and the lead compounds were characterized for oral bioavailability, lack of *in vitro* off-target effects, *in vivo* safety, and suitability for pharmaceutical formulation. The final candidate identified from over 3,500 compounds synthesized and evaluated was ataluren (3-[5-(2-fluorophenyl)-[1,2,4]oxadiazol-3-yl]-benzoic acid, clinical name, PTC124), a 284-Dalton small molecule compound that is orally bioavailable and distinct in structure from aminoglycosides, which as previously discussed are known to have premature stop codon readthrough activity as well. Ataluren has no antibacterial activity since the compound does not inhibit the growth of bacteria that are otherwise susceptible to antibiotics of the aminoglycoside or ampicillin classes.

Exhibit 7. Structure Of Ataluren



Source: PTC Therapeutics, Inc.

Preclinical studies demonstrated that ataluren's activity is both potent and selective. It promotes dose-dependent readthrough of all three premature stop codons based on luciferase assay data although efficiency was the highest for UGA, followed by UAG and UAA. Compared to gentamicin, an antibiotic that belongs to the aminoglycoside family, ataluren achieves a higher degree of premature stop codon readthrough at a significantly lower concentration. Therefore, ataluren appears to be a much more potent readthrough agent than aminoglycosides.

PTC conducted *in vitro* assays across multiple exons in different genes and demonstrated that the induction of premature stop codon readthrough by ataluren is not dependent on the location of the nonsense mutation. Therefore, ataluren has the potential to be a universal agent that can be used for nonsense mutation suppression for the treatment of other genetic disorders. In fact, this potential has been well supported by studies conducted by both PTC and other independent investigators in other disease models in addition to nmDMD and nmCF.

Ataluren Affects Premature But Not Normal Stop Codons

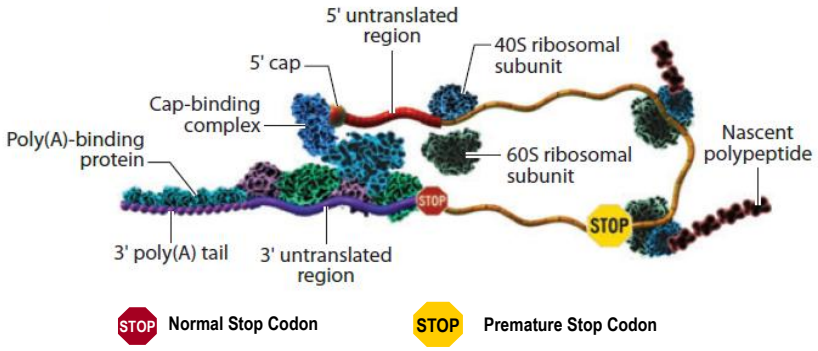
Ataluren induces readthrough of only premature but not normal stop codons. The high specificity, which is extremely important in preventing the production of aberrant proteins, is due to the structural difference between a premature stop codon and a *bona fide* stop codon. A

normal stop codon is followed by the 3'-un-translated region (3'-UTR) and a poly(A) tail that consists of multiple adenosine monophosphates whereas a premature stop codon has neither.

The NMD pathway, which rapidly degrades transcripts containing premature stop codons, distinguishes premature stop codons from natural stop codons based on their locations relative to downstream sequence elements such as a properly configured 3'-UTR, associated proteins that provide position information, and possibly other unidentified mechanisms. Likewise, ataluren and aminoglycosides may utilize similar information in specifically recognizing premature stop codons when inducing readthrough.

Additionally, many mRNAs have a second stop codon in the 3'-UTR regions, downstream but in proximity to the first physiological stop codon. This feature provides another layer of protection in the prevention of non-specific readthrough since *in vitro* assays have demonstrated that ataluren is not able to induce readthrough of tandem stop codons.

Exhibit 8. Premature Stop Codons Are Distinct From Normal Stop Codons



Source: PTC Therapeutics, Inc.

Given the importance of this specificity, PTC has conducted extensive studies to confirm that ataluren induces readthrough of only premature stop codons but not normal stop codons. No protein products from readthrough of physiological stop codons were detected either from cultured mammalian cells after ataluren treatment or from tissues isolated from ataluren-treated human subjects and animals. PTC identified multiple rat, dog and human genes that can produce elongated proteins if readthrough at the normal stop codons occurs. In both rats and dogs, no elongated protein products of selected genes were detected after ataluren administration. In healthy human volunteers, ataluren was administered at 50mg/kg BID (a dosage much higher than what was used in clinical trials to date) for 14 days and peripheral blood mononuclear cells (PBMCs) were collected on day 14 at various time points as well as three days after the last dose. Protein assays conducted on samples prepared from the PBMCs revealed no detectable non-specific readthrough of normal stop codon in the *beta2-microglobulin* gene and a few other genes selected for the assay.

The high specificity of ataluren's activity in inducing readthrough of premature stop codons only, without affecting the NMD pathway, may have also contributed to the strong safety profile of ataluren observed in subsequent clinical trials by causing no disturbance to important genomic surveillance pathways.

Mechanism Of Action Of Ataluren: Likely Through Ribosomal Binding

Suppression of nonsense mutations via premature stop codon readthrough could result from either increased stabilization of mRNAs that contain premature stop codons (through inhibition of the NMD pathway) or an alteration of translation termination efficiency, or the combination of both. Ataluren targets only translation and does not affect the NMD pathway. An increase in premature codon readthrough was measured in the initial screening and in subsequent *in vitro* assays which confirmed that ataluren has no effect on mRNA levels. In comparison, cycloheximide, a protein synthesis inhibitor that is well known to stabilize mRNAs, induced an over ten-fold increase in mRNA levels in the same assays. Therefore, ataluren is more likely to be functioning on the termination efficiency at the premature stop codons.

The most reasonable hypothesis would be that ataluren has a similar mechanism of action as the aminoglycosides of binding to the same decoding region of the ribosomes in promoting premature stop codon readthrough. This hypothesis is well supported by an observation from clinical trials where the co-administration of aminoglycosides, but not other classes of antibiotics that don't have activity in inducing premature stop codon readthrough, attenuated ataluren's efficacy. This observation can be explained by the competition between ataluren and aminoglycosides for the same binding site within the ribosomes and aminoglycosides' less potent activity in inducing premature stop codon readthrough.

Debate On Readthrough Efficacy: *In Vivo* Data Should Prove More Definitive

In June 2013, an article was published in the journal *of PLOS Biology* questioning the mechanism of action of ataluren in inducing readthrough of nonsense mutations. The authors of the article conducted multiple *in vitro* reporter assays in a cultured cell line which demonstrated no detectable readthrough activity and led the authors to conclude that ataluren lacks premature stop codon readthrough efficacy.

The *PLOS Biology* article questioned the luciferase assays that PTC utilized for the identification of the initial candidate chemical scaffolds. However, assays conducted by the authors are based on complementary DNA (cDNA, is a form of DNA synthesized from mRNA templates) overexpressed or stably expressed in cultured cell lines. This creates a highly artificial experimental setting and as a result, the data may demonstrate significant variation depending on the agents (including cultured cells) used and the protocol followed. Specifically, the AD293 cell line used in the *PLOS Biology* article was derived from the human embryonic kidney (HEK) 293 cells, which were used for the initial identification of ataluren. However, the

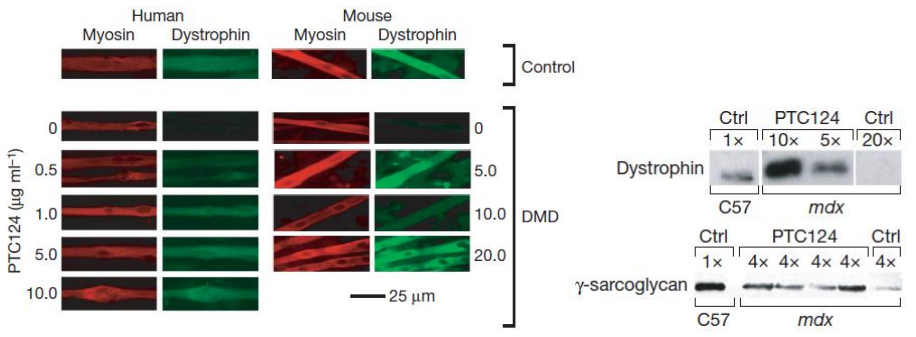
two cell lines (AD293 vs. HEK293) have demonstrated different gene expression profiles as well as contrasting cellular reactions to identical stimuli.

The use of cDNA instead of natural mRNA may have also affected the assay's sensitivity to premature stop codon readthrough. Premature stop codon recognition is known to be dependent on the exon junction complex (EJC), a group of proteins that bind to mRNA after splicing – the process that connects exons (regions inside a gene that contain genetic information which will be transmitted from DNA to protein) that were originally separated by introns (regions that do not participate in the production of the protein). Genes that do not contain introns, much like cDNA, are insensitive to premature stop codon recognition by cellular machineries, therefore, the assay setup in the *PLOS Biology* article is not ideal.

The validation steps that led to the final clinical development of ataluren are much more important in confirming the mechanism of action of ataluren, in our opinion, and PTC has generated an abundant amount of data in support of ataluren's activity in inducing effective readthrough of premature stop codons and in restoring production of full-length proteins.

In primary muscle cell cultures derived from both nmDMD patients and *mdx* mice, which carry nonsense mutations in the dystrophin gene and therefore are often used as an animal model for the disease, ataluren treatment induced production of full-length dystrophin in myotubes as indicated by immunohistochemistry studies using a dystrophin antibody that recognizes an epitope located at the carboxy-terminus of the protein. Western blot, the most commonly used method for protein detection, demonstrated that full-length dystrophin was produced in the muscles isolated from *mdx* mice that were treated with ataluren. Moreover, ataluren treatment also increased the protein levels of gamma-sarcoglycan, a member of the dustrophin-associated glycoprotein complex that is important for the normal function of dystrophin. Since loss of the dystrophin protein results in the disappearance of the entire protein complex, an increase in gamma-sarcoglycan provides additional and solid evidence that full-length dystrophin is being produced and newly produced protein is functional.

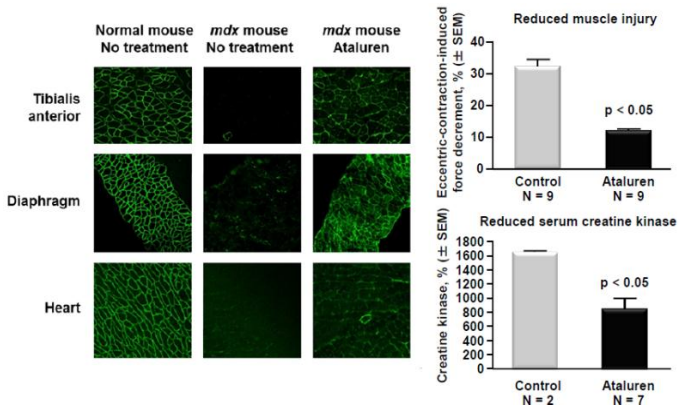
Exhibit 9. Full-Length Dystrophin Production In Cultured Myotubes After Ataluren Treatment



Source: PTC Therapeutics, Inc.

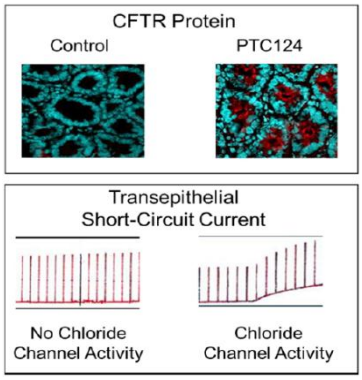
PTC swiftly proceeded into preclinical studies using animal models of genetic diseases after the identification of ataluren. We believe that *in vivo* data in animal models demonstrating production of full length proteins provides the strongest evidence supporting the activity of ataluren in inducing readthrough of premature stop codons and restoring protein production. In *mdx* mice, treatment with ataluren partially restored dystrophin production in skeletal muscles which included tibialis anterior muscles and diaphragm muscles as well as in cardiac muscles. More importantly, novel dystrophin was found correctly localized at the sarcolemma that surrounds muscle fibers, suggesting that the protein should have physiological functionality as well. In a CF model that carries a nonsense mutation in the disease causing *CFTR* gene, ataluren treatment led to the expression of full-length CFTR protein at the apical surface intestinal glands as was detected with immunofluorescence staining with an antibody against the protein. Moreover, functional assays measuring the average cyclic AMP (cAMP)-stimulated transepithelial chloride currents demonstrated ataluren-treated CF mice achieved 24% to 29% functional recovery as compared to wild-type mice. Therefore, there is a large amount of *in vivo* and functional data that support ataluren's mechanism of action.

Exhibit 10. Ataluren Restores Dystrophin Production As Well As Correct Protein Localization



Source: PTC Therapeutics, Inc.

Exhibit 11. Ataluren Restores CFTR Protein Production As Well As Ion Channel Function



Source: PTC Therapeutics, Inc.

Furthermore, numerous independent studies conducted by third parties, as listed in the chart that follows, most of them in animals or in human tissues, have also provided robust evidence supporting ataluren's activity in inducing premature stop codon readthrough and restoring target protein production. The disease models studied for ataluren include Usher syndrome, carnitine palmitoyltransferase 1A deficiency, Batten disease, mucopolysaccharidosis VI, pulmonary arterial hypertension, ataxia telangiectasia, and pseudoxanthoma elasticum.

Exhibit 12. Literature Supporting Ataluren's Activity

- Cell-based and cell-free reporter assay activity
  - Activity is stop codon dependent (Welch et al., 2007)
- Demonstrated nonsense suppression in several model systems
  - Mdx and human myotubes (full-length protein produced; Welch et al., 2007)
  - Mdx mice (full-length protein and functional benefit; Welch et al., 2007)
  - Xenograft model (CaOv3 cells; p53 nonsense allele) – tumor reduction
  - Hurler mouse model (protein activity and GAG reduction)
  - Cftr transgenic mice (full-length protein and functional benefit; Du et al., 2008)
  - Miyoshi dysferlinopathy: Dysferlin (Wang et al. *J. Appl Physiol* **109**: 901, 2010)
  - Carnitine palmitoyltransferase 1A deficiency: CPT1A (Tan et al., J. Inherit. Metab. Dis., 2011)
  - Usher syndrome: USH1C (Goldmann et al., Human Gene Ther., 2011)
  - Batten disease - INCL (Sarkar, et al., Mol. Genet. Metab. 2011)
  - MPSVI – ARSB (Bartolomeo et al., J Inherit Metab Dis. 2012)
  - MoLV - gag-pol readthrough (Green et al., Columbia Univ. Thesis, 2012)

Source: PTC Therapeutics, Inc.

Another noteworthy factor that may affect the efficacy in nonsense mutation suppression, as suggested by studies conducted with aminoglycosides, is the source of the chemical compound. For example, three variants of gentamicin that only differ slightly in their chemical structures have demonstrated significant differences in their activity to induce premature stop codon readthrough. Investigators have noted the importance of using aminoglycosides produced from the same source for clinical trials since compounds manufactured under the same condition provide much better consistency for data interpretation whereas gentamicin compounds from difference sources have produced inconsistent results in independent clinical trials. We believe that the same theory applies to the different ataluren compounds used in PTC's studies and in the *PLOS Biology* study.

In summary, we believe that the concerns raised by the recent *PLOS Biology* article against the activity of ataluren are over-stated and that there is significantly more abundant and more convincing evidence to support ataluren's activity in suppressing nonsense mutations than to argue against it. Investor focus should be on whether ataluren will be able to demonstrate meaningful clinical benefit in the ongoing confirmatory Phase III clinical trial in DMD and the planned confirmatory Phase III trial in CF, in our opinion, since the NDA filing will be supported by and the decision regarding regulatory approvals will be based on results from these clinical trials.

Duchenne Muscular Dystrophy (DMD)

PTC is developing ataluren for Duchenne Muscular Dystrophy (DMD) and cystic fibrosis (CF). DMD is a fatal neuromuscular disorder and is the most severe form of muscular dystrophy, characterized by the early onset of muscle degeneration and wasting. Patients suffer from progressive muscle weakness and eventually become completely paralyzed. Cardiomyopathy and breathing difficulties usually begin by the age of 20 and patients typically die from respiratory failure or lung disorders by age 25.

Epidemiology

DMD is an X-linked genetic disorder that affects approximately one in 3,500 newborn boys. The disease is caused by mutations in the dystrophin gene (DMD gene) located in the short arm of the X chromosome. Female carriers usually demonstrate much milder symptoms or are asymptomatic since they have two X chromosomes. In rare cases associated with chromosomal rearrangement or skewed X chromosome inactivation, affected girls can have disease severity comparable to that seen in affected boys.

Symptoms

DMD patients typically develop muscle weakness in the early years of life. The severe muscle wasting and weakness become clinically evident between the ages of three and five years. Although DMD patients can continue to make progress in motor function until approximately four to six years of age, typically at a slower rate than their healthy peers, they lose their independent ambulation and become wheel chair bound in their early teens. DMD patients progress to develop respiratory, orthopedic, and cardiac complications and if left untreated, will die in their early twenties. Non-progressive cognitive dysfunction may also emerge with the progress of the disease. Even with assisted ventilation, the life expectancy is less than 30 years.

Diagnosis And Management Of DMD

Most DMD patients are diagnosed around the age of five when their symptoms due to physical inability become evident. An accurate and prompt diagnosis is important since it allows for early initiation of appropriate palliative therapies. The DMD Care Considerations Working Group, a group of 84 clinicians selected by the U.S. Centers for Disease Control and Prevention (CDC) to develop care recommendations for DMD, suggests that the suspicion of DMD diagnosis should be considered when one of the following three observations is made, irrespective of family history:

- The observation of abnormal muscle function in a male child.
- The detection of an increase in serum creatine kinase tested for unrelated indications. Creatine kinase is clinically assayed as a marker of muscular dystrophy as well as several other muscle-related disorders since an elevation of the creatine kinase level is an indication of muscle damage.
- After the discovery of increased transaminases (aspartate aminotransferase (AST) and alanine aminotransferase (ALT), which are produced by muscle as well as liver cells). Elevated transaminase levels (especially AST) can be caused by strenuous exercise or myopathy.

The key tests performed on muscle biopsy samples are immunocytochemistry and immunoblotting to detect dystrophin protein, which is mostly absent in DMD patients. To confirm a diagnosis of DMD, a genetic test of the DMD mutation in a blood sample is always necessary even when there is an absence of dystrophin protein in muscle biopsy samples. Although a muscle biopsy is not necessary if a genetic diagnosis is confirmed first, a genetic test is mandatory even after a positive biopsy diagnosis. Complete characterization of the mutation(s) will provide valuable information for future mutation-specific treatments.

No disease modifying treatments are available for DMD. Corticosteroids, currently the only available medication, and physical therapy are used to slow the decline in muscle strength and to prolong ambulation in DMD patients. Clinical studies have demonstrated the beneficial effects of prednisone treatment in DMD patients and based on the positive results, the DMD Care Considerations Working Group strongly recommends the consideration of glucocorticoid therapy in all DMD patients, except those who are still gaining motor skills or are younger than two. Additional respiratory, orthopedic, cardiac and rehabilitative interventions can also improve the health, quality of life, and lifespan of DMD patients.

Six-Minute Walk Test (6MWT), The Ultimate Function Assessment

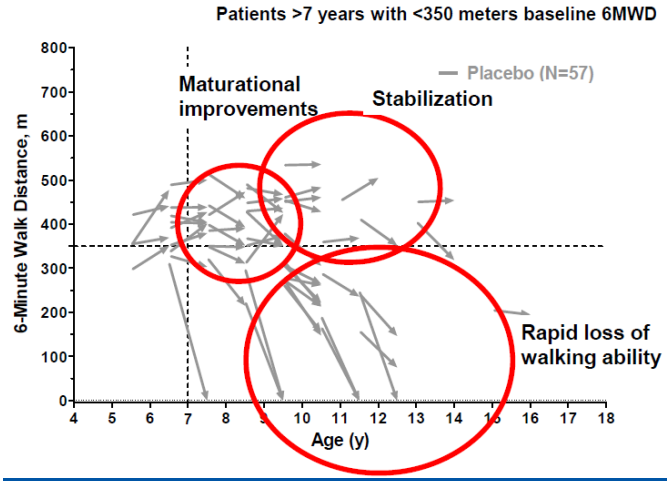
The 6MWT is a widely employed test due to its ease of administration, better tolerance, and better reflection of daily activities. The American Thoracic Society Pulmonary Function Standards Committee developed guidelines for the 6MWT in clinical settings. A wide range of indications can be measured with the 6MWT and the most important assessment is to compare outcomes before and after treatment in patients with moderate to severe heart and lung disease. But muscle strength and musculoskeletal disease can also be measured. The total distance walked is the primary measure of the 6MWT. Healthy subjects' 6MWT distance range from 400 to 700 meters and the distance can be influenced by gender, age, height, and body weight.

Natural History Studies Provide The Most Reliable Database

Extensive natural history studies have been conducted to characterize disease progression in DMD patients who are not receiving medical intervention. The results indicate that age and baseline walking ability as measured by the 6MWT are the two most important factors that would predict a patient's disease progression. Patients younger than seven tend to demonstrate improvement in their walking ability even without any medical intervention because they are still gaining muscle strength in early development. In contrast, patients above the age of seven either remain stable or demonstrate rapid deterioration. A baseline walking distance of 350 meters appears to be the border line that predicts patients' potential performance in clinical trials: people who are able to walk more than 350 meters at baseline tend to maintain their walking ability throughout the trial period whereas people who are not tend to demonstrate a rapid decline.

These findings from natural history studies were confirmed in PTC's Phase IIb clinical trial in nmDMD patients and have been instrumental in the design of the confirmatory Phase III clinical trial.

Exhibit 13. The Six-Minute Walk Distance (6MWD) Based On Age And Baseline Performance



Source: PTC Therapeutics, Inc.

Dystrophin

The dystrophin gene (DMD gene) was identified in 1986 and is the largest human gene that has been characterized to date. It has a total of 79 exons separated by introns, many of which exceed several hundred kilobases in length. The entire gene is spread over 2.6 million base pairs in the genome. Dystrophin is expressed in all three types of muscles: skeletal, smooth, and cardiac muscle, and in the central nervous system as well.

In muscle cells, dystrophin protein is localized to the sarcolemma, the membrane structure that consists of the plasma membrane and a thin layer of polysaccharide material, and functions as a link between the cytoskeleton and extracellular matrix in the muscle. The main function of dystrophin is to provide stabilization to muscle fibers and to protect them from the mechanical forces of muscle contraction. Additionally, dystrophin may function in cell signaling transduction. When dystrophin is missing, sarcolemma becomes detached from the cytoskeleton and loses synchronization with the interior of the muscle cell during muscle contraction. This in turn causes the calcium channels on the membranes to open and the inflow of calcium ions activates the proteolytic enzyme calpain which digests intracellular proteins such as those important for contraction. As a result, progressive damage and necrosis of muscle fibers occurs and the muscle becomes weaker. Dystrophin is also expressed in nerve cells but the function of dystrophin in the nervous system is not well understood.

Dystrophin-Associated Glycoprotein Complex (DGC)

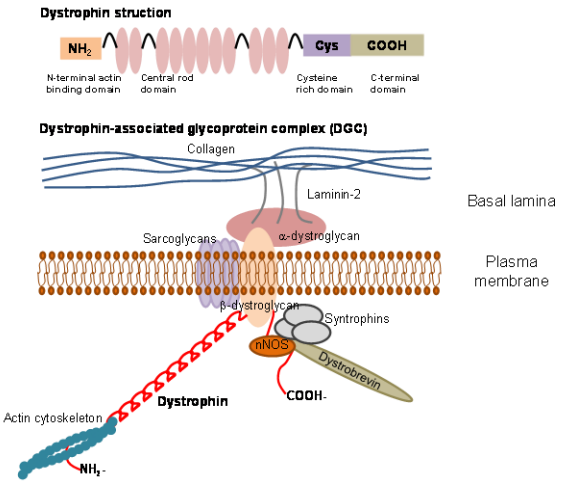
Dystrophin is associated with a large protein complex of sarcolemmal proteins and glycoproteins in linking the cytoskeleton and extracellular matrix and maintaining normal muscle function. The association is mediated through four main functional units within the dystrophin protein:

- The N-terminus where the binding site for actin is located
- The central rod domain that contains 24 triple helical spectrin repeats
- The cysteine-rich domain to the C-terminus
- The C-terminal domain. Both the cysteine-rich domain and the C-terminal domain are required for the binding between dystrophin and its interacting proteins.

The DGC contains three sub-complexes:

- The alpha-dystroglycan and beta-dystroglycan that connect the cysteine-rich domain and the first half of the carboxyl-terminal domain of dystrophin to the extracellular matrix
- The sarcoglycans that are embedded in the muscle plasma membrane and their constitution differs across different muscle types
- Syntrophin, nNOS, and dystrobrevin which all bind to the second half of the carboxyl-terminal domain of dystrophin and may function to regulate the intracellular signaling pathway through their binding with the DGC.

Exhibit 14. Dystrophin Structure And Interaction With The DGC



Source: Cowen and Company

Dystrophin is essential for the stability of the DGC and loss of the dystrophin protein in humans results in the disappearance of the entire protein complex. Neuronal nitric oxide synthase (nNOS), a protein that binds directly to dystrophin and regulates the blood flow in skeletal muscle, loses membrane localization in DMD patients. The lack of nNOS at the sarcolemmal membrane is thought to be the reason for ischemia following exercise, which in turn causes additional muscle tissue damage in DMD.

Becker Muscular Dystrophy (BMD)

Becker Muscular Dystrophy (BMD) is a milder disorder caused by mostly in-frame mutations in the same *DMD* gene. Since mutations do not change the reading frame, production of dystrophin protein, although in a truncated form, is preserved. Although some BMD patients also lose the ability to walk in their late teens or early twenties as DMD patients do, other BMD patients can be asymptomatic and do not experience functional difficulties. Overall, the majority of BMD patients are able to retain ambulation and to maintain a normal lifespan. Due to the technical challenges in genotyping patients, PTC did not separate nmBMD patients from nmDMD patients when enrolling patients for the earlier clinical studies. The company does not plan to actively separate patients by disease type for the ongoing confirmatory Phase III clinical trial. However, based on the redefined inclusion criteria, we believe that very few, if any, BMD patients will be enrolled.

Clinical Trial History In nmDMD

Phase I Studies Demonstrate Safety And Tolerability

PTC conducted two Phase I studies of ataluren, one escalating single-dose trial and the other an escalating multiple-dose trial, in a total of 63 healthy adult volunteers. Both studies were conducted at a single center in the U.S. The single dose study evaluated six dose levels of ataluren, ranging from 2mg/kg to 300mg/kg whereas the patients in the multiple-dose study received twice-daily administration of ataluren at 10, 20, 30, and 50mg/kg/dose. Ataluren was generally safe and well-tolerated, with adverse events being mild to moderate.

Most importantly, no protein elongation due to non-specific ribosomal readthrough of normal stop codons was detected. Peripheral blood mononuclear cells (PBMC) and plasma samples from the single dose study and the multiple dose study were pooled respectively and were examined for the presence of elongated forms of C-reactive protein (CRP), beta-2 microglobulin and cystatin C, all of which are representative proteins found in the blood. No elongated forms of any of these proteins were detected, suggesting that ataluren treatment does not induce non-specific readthrough of normal stop codons.

Phase IIa Clinical Trial Confirms Proof Of Concept

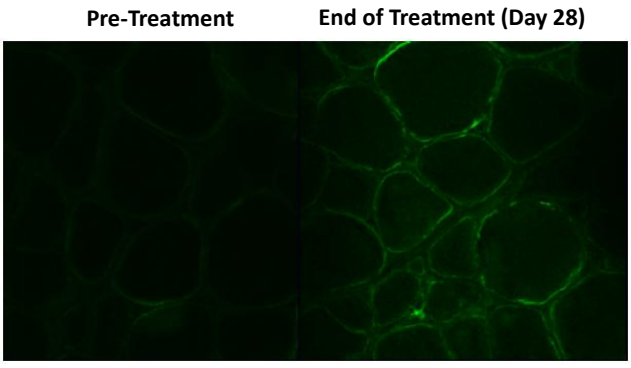
In December 2005, PTC initiated an open-label Phase IIa clinical trial to assess ataluren-induced dystrophin production in nmDMD patients. The trial evaluated 28 days of ataluren administration dosed three times per day at three dose levels:

- 4mg/kg after breakfast, 4mg/kg after lunch and 8mg/kg after dinner (low dose)
- 10mg/kg, 10mg/kg and 20 mg/kg on the same dosing schedule (mid dose)
- 20mg/kg, 20mg/kg and 40 mg/kg on the same dosing schedule (high dose)

The trial enrolled a total of 38 patients above the age of five at three U.S. academic centers. The first six patients received the low dose; the following 20 patients received the mid dose; and the final 12 patients received the high dose. The primary endpoint of the trial was dystrophin protein level change from baseline as assessed by immunofluorescence staining of biopsy tissues from the extensor digitorum brevis (EDB) muscle of the foot. The comparison was conducted between the entire EDB muscle that was removed from one foot prior to treatment and the EDB muscle from the other foot that was removed after treatment. Second endpoints of the trial included safety and tolerability, muscle function, serum CK levels, compliance with ataluren treatment and ataluren pharmacokinetics.

Ataluren induced an average 11% increase in muscle dystrophin expression over the 28 days of treatment with 23 of the 38 patients (61%) demonstrating an increase of dystrophin levels from baseline. Serum CK reductions were observed in 35 of the 38 patients (92%) at the end of the 28-day treatment period. Muscle function as measured with myometry scores and timed function tests did not demonstrate a statistical significant improvement with 28 days of ataluren treatment although there were anecdotal reports of greater activity, increased endurance and less fatigue in ataluren treated patients.

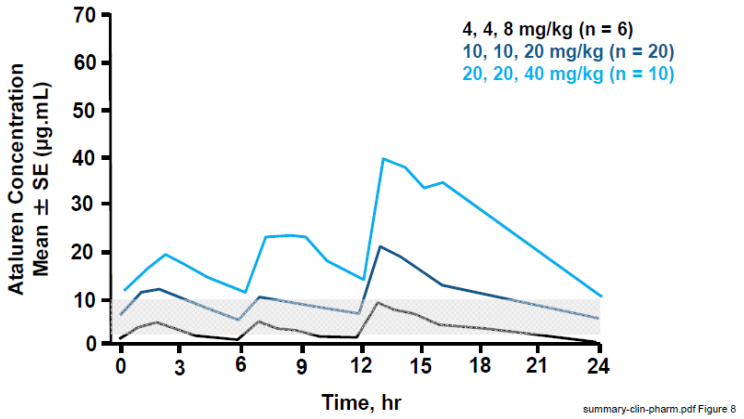
Exhibit 15. Ataluren Treatment Increases Dystrophin Protein Production



Source: PTC Therapeutics, Inc.

Preclinical studies conducted in the DMD mouse model suggest that a plasma level that is maintained at above 10ug/mL is required for ataluren to demonstrate a therapeutic effect. Pharmacokinetic results from the Phase IIa clinical trial indicated that both the mid dose (10,10,20mg/kg) and high dose (20,20,40mg/kg) achieved this plasma concentration. These two doses were further evaluated in the subsequent Phase IIb clinical trial.

Exhibit 16. Phase IIa: Ataluren Demonstrates Dose-Dependent Plasma Concentration



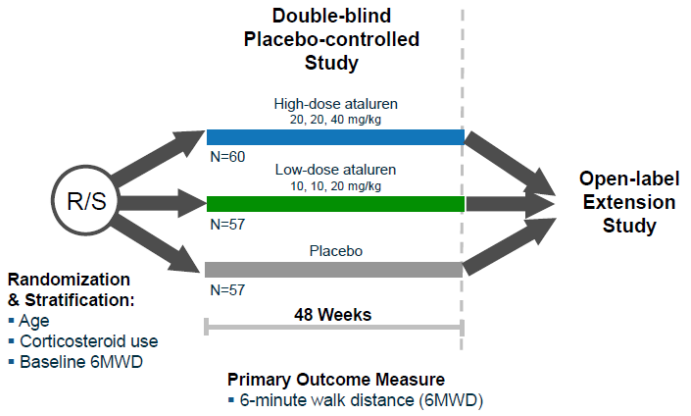
Source: PTC Therapeutics, Inc.

Phase IIb Clinical Trial Demonstrates A Highly Promising Trend

The randomized, double-blind, placebo controlled, dose ranging Phase IIb clinical trial evaluated the long-term efficacy and safety of ataluren in a total of 174 nmDMD patients who were at least five years of age at 37 investigational sites in 11 countries. The patients were required to walk at least 75 meters without any assistance to be enrolled in the trial. Corticosteroid treatment was not required for enrollment but patients receiving corticosteroids were required to have been on the therapy for at least six months prior to enrollment and to have been on a stable dosing regimen for at least three months before entering the trial. The patients were randomized 1:1:1 into the following three treatment cohorts:

- Ataluren three times per day, in the morning, at midday, and in the evening at 10mg/kg, 10mg/kg, and 20mg/kg, respectively
- Ataluren on the same schedule but at 20mg/kg, 20mg/kg, and 40mg/kg, respectively
- Placebo

Exhibit 17. Phase IIb Clinical Trial Design



Source: PTC Therapeutics, Inc.

The primary endpoint of the study was the mean change in the 6-minute walk distance (6MWD) at week 48 as compared to baseline. Patients made clinical visits every six weeks to have treatment efficacy and safety assessed. The primary endpoint analysis was conducted in the intent-to-treat (ITT) population from the 174 patients enrolled in the trial. Secondary endpoints included additional muscle function tests, muscle strength measurement, bicep muscle dystrophin expression, among other endpoints. The Phase IIb clinical trial also included supportive analyses of ambulation as measured with the proportion of patients with at least 10% worsening in the 6MWD at week 48 when compared to baseline and the time to persistent 10% worsening in the 6MWD from baseline.

In March 2010, PTC announced preliminary results from the Phase IIb clinical trial. The trial failed to meet the primary endpoint of a statistically significant change in the 6MWT distance from baseline after 48 weeks of treatment.

Subsequently in October 2011, PTC announced that final analyses of the Phase IIb trial results demonstrated some clinical benefit from low-dose ataluren treatment. The patients who received low-dose ataluren walked an average of 29.7 meters more in the 6MWT than the patients in the placebo cohort (p=0.058). However, there was no difference between the high-dose cohort and the placebo cohort and all cohorts' walking distance declined over the course of the trial. Low-dose ataluren treatment also demonstrated a certain level of disease progression. However, PTC stated that the secondary endpoint of dystrophin expression levels could not be properly assessed partly due to technical limitations and that no relationship could be established between dystrophin levels and the 6MWT performance.

Post Hoc Analysis Brings P Value Closer To Statistical Significance

The 6MWT distances demonstrated in the Phase IIb clinical trial did not follow a symmetric normal distribution, which is required for a number of commonly used statistical tools such as

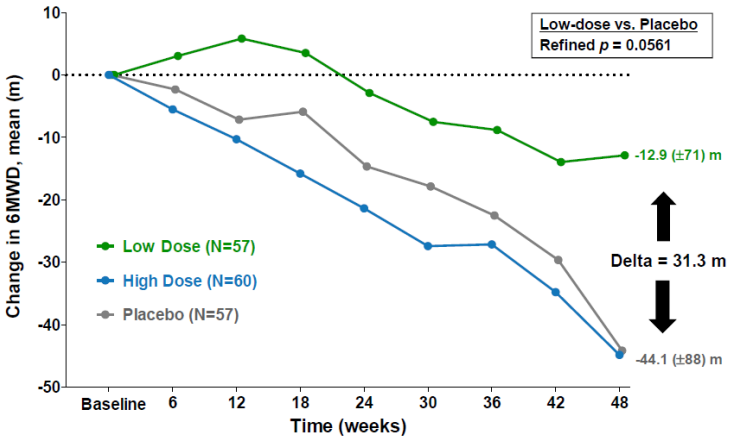
the *t*-test. One of the most frequent reasons for non-normality is the existence of extreme values which occurred in the ataluren Phase IIb clinical trial.

We believe that the larger than expected variation observed in the DMD patients enrolled in the Phase IIb clinical trial was the major reason why the trial failed to achieve statistical significance in the primary endpoint measurement. The standard deviations from the placebo and low-dose ataluren cohorts were 90 meters and 72 meters, respectively. Natural history studies have suggested that disease progression is highly dependent on patients' age and baseline walking ability. However, the Phase IIb trial enrolled a rather heterogeneous patient population, ranging from five to 20 in age and there was not an upper limit in the baseline walking ability. As a result, the standard deviation was much higher than the assumed 50 meters. With only 57 patients enrolled in each of the low-dose ataluren cohort and placebo cohort, the Phase IIb clinical trial did not have enough power to reach statistical significance even though results demonstrated a clear trend of improvement in the 6MWT performance in the patients who received low-dose ataluren treatment.

PTC conducted a *post hoc* analysis of the data with a modified statistical analysis method to minimize the negative impact from the outliers. The pre-specified analysis of the 6MWT data ranked the 6MWD for each patient from the smallest to the largest and replaced the actual meters that each patient walked during the 6MWT with a number from one to 174. This ranking method provides a relative order of each patient's performance; however, it failed to reflect the significant variability observed in the Phase IIb clinical trial.

PTC performed a re-randomization test to analyze the patients' 6MWD data in actual meters to address the issue of non-normality. The modified statistical analysis generated a p value of 0.0561 from a clinical benefit of approximately 31.3 meters from low-dose ataluren treatment as compared to placebo.

Exhibit 18. Low-Dose Ataluren Treatment Resultes In Clinical Benefit



Source: PTC Therapeutics, Inc.

The magnitude of clinical benefit ataluren demonstrated in the Phase IIb clinical trial was comparable to FDA approved therapeutics that target similar neuromuscular disorders, which on average demonstrated clinical benefits of approximately 30 meters in their registration trials. Therefore, we believe that a U.S. regulatory approval is highly possible should ataluren replicate the clinical benefit in the ongoing confirmatory Phase III clinical trial.

Exhibit 19. Ataluren Demonstrates A Comparable Clinical Benefit

Therapeutic	Indication	Treatment duration (week)	Mean improvement in 6MWT compared to placebo (meter)	Price
Ataluren	DMD	48	30	-
Aldurazyme	MPS I	26	38	$282,000*
Elaprase	MPS II	53	35	$411,000*
Myozyme	Pompe	78	23	$355,000*

* Based on a 35kg patient;

Source: MME, LLC & Price Rx

Additional Endpoint Analyses Support A Clinical Benefit

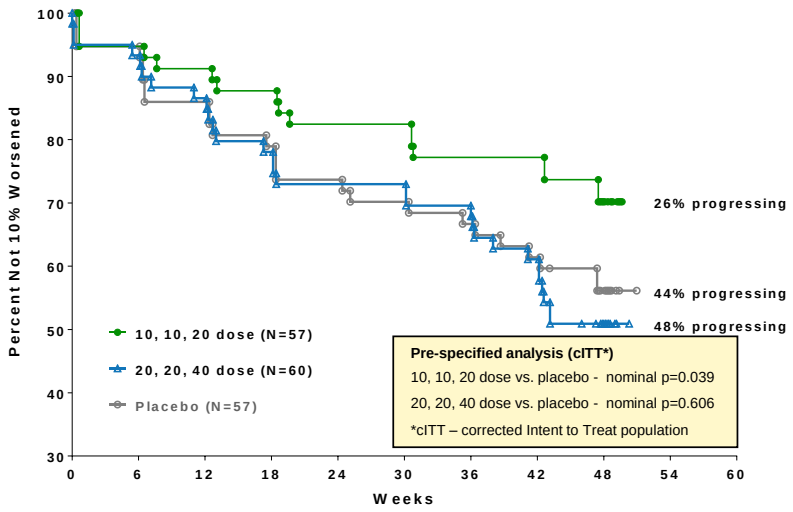
PTC included the following two additional endpoints in the Phase IIb clinical trial.

- The proportion of patients with at least 10% persistent worsening in the 6MWD at week 48 as compared to baseline
- Time to 10% persistent worsening in the 6MWD from baseline

The pre-specified 10% persistent worsening in the 6MWD generally predicts a substantial decline in a patient's clinical condition over the subsequent years and therefore is a clinically meaningful criterion. Similar to the primary endpoint analysis of the 6MWD, low dose ataluren treatment failed to reach statistical significance in the first additional endpoint analysis as compared to placebo but demonstrated a positive trend. Approximately 26% of the patients who received low dose ataluren, as compared to approximately 48% of placebo-treated patients, experienced at least 10% persistent worsening in the 6MWD after 48 weeks of treatment (p=0.039).

The second pre-specified endpoint, time to 10% persistent worsening, did not demonstrate any statistical significance or trends among the three treatment cohorts.

Exhibit 20. Low-Dose Ataluren Slows Disease Progression

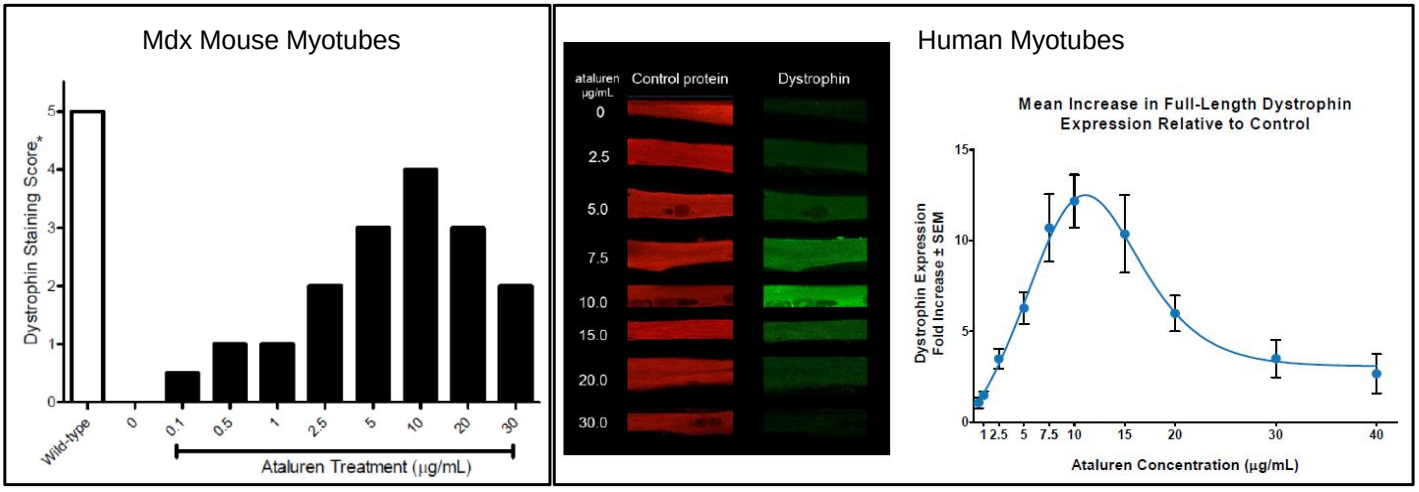


Source: PTC Therapeutics, Inc.

Bell-Shaped Curve: Well Supported By Extensive Characterization

Ataluren demonstrated an interesting reverse dose response in the Phase IIb clinical trial, with the lower dose regimen demonstrating a better clinical benefit than the higher dose. The bell-shaped curve was replicated in subsequent *in vitro* studies conducted by PTC using myotubes isolated from both disease model mice and nmDMD patients – a lower concentration of ataluren demonstrated a better efficacy in inducing dystrophin production. Therefore, we believe the observation is related to the mechanism of action of ataluren.

Exhibit 21. Bell-Shaped Ataluren Dose-Response Curve In Dystrophin Expression In Treated Myotubes

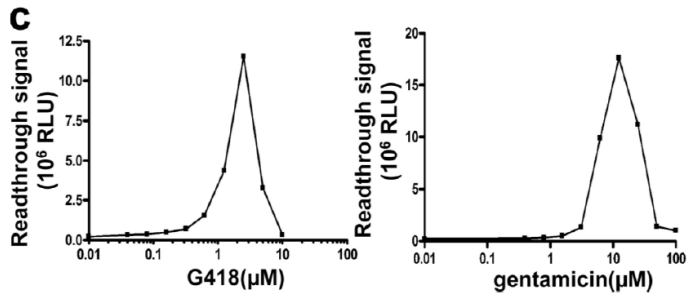


Source: PTC Therapeutics, Inc.

Similarly, *in vitro* data from embryonic fibroblasts from a Hurler mouse model and *in vivo* data from the same mice demonstrated a bell-shaped ataluren dose-response curve in the reduction of glycosaminoglycans (GAGs).

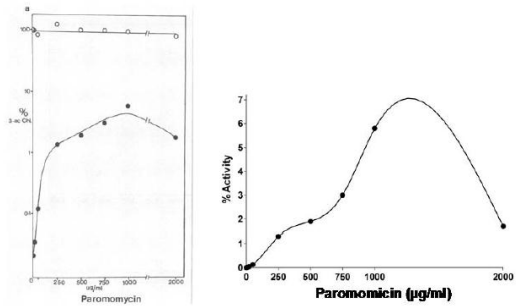
A similar bell-shaped curve has been observed from aminoglycosides as well. PTC has hypothesized that there are two potential binding sites within the ribosome for aminoglycosides and has proposed the following model: at low concentrations, aminoglycosides bind to the high-affinity site and induce premature stop codon readthrough whereas at higher concentrations, they begin to occupy the low-affinity site and this binding interferes with readthrough activity. Given the possibility that ataluren binds to the same site(s) of the ribosome, we believe that the bell-shaped curve observed in the ataluren Phase IIb clinical trial is a natural phenomenon and we feel comfortable that PTC has identified an effective, if not the optimal dose of ataluren.

Exhibit 22. Bell-Shaped Curve In Readthrough Induced By Aminoglycosides



Source: PTC Therapeutics, Inc.; Du et al., *J. Exp. Med*., 2009

Exhibit 23. Bell-Shaped Curve In Paromomicin-Mediated Suppression Of Nonsense mRNA



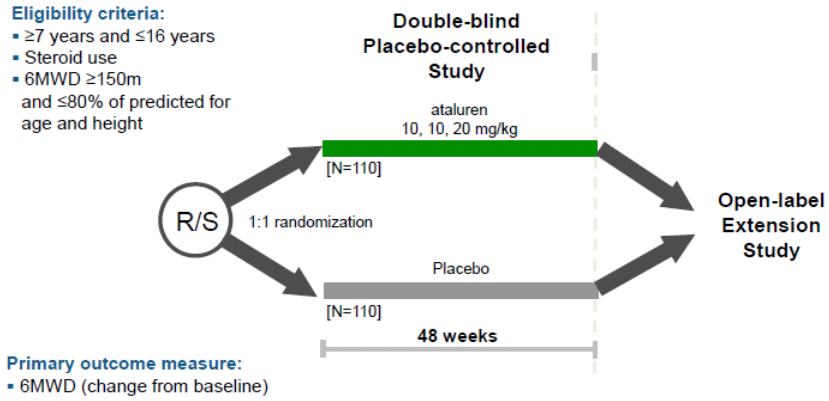
Source: PTC Therapeutics, Inc.; Burke and Mogg, *Nucleic Acid Research*, 1985

Confirmatory Trial In nmDMD Is Ongoing

PTC has initiated a confirmatory Phase III clinical trial of ataluren for the treatment of nmDMD and dosed the first patient in April 2013. The global randomized, double-blind, placebo-controlled trial will evaluate the efficacy and safety of ataluren in approximately 220 nmDMD patients. PTC expects to report top-line data in mid-2015.

The primary endpoint of the confirmatory trial is the same as in the Phase IIb clinical trial: the clinical benefit of ataluren treatment on patients' walking ability as measured with the 6MWT. Secondary endpoints will include assessment of physical function and quality of life. However, the patient enrollment criteria were modified based on what PTC learned from the *post hoc* analysis of the Phase IIb data to increase the possibility of success.

Exhibit 24. Confirmatory Phase III Clinical Trial Design



Source: PTC Therapeutics, Inc.

PTC expects to complete the Phase III confirmatory study and report top-line data in mid-2015. An open-label extension study will follow the double-blind treatment period.

Post Hoc Analysis Of Phase IIb Increases Chances Of Success In Phase III

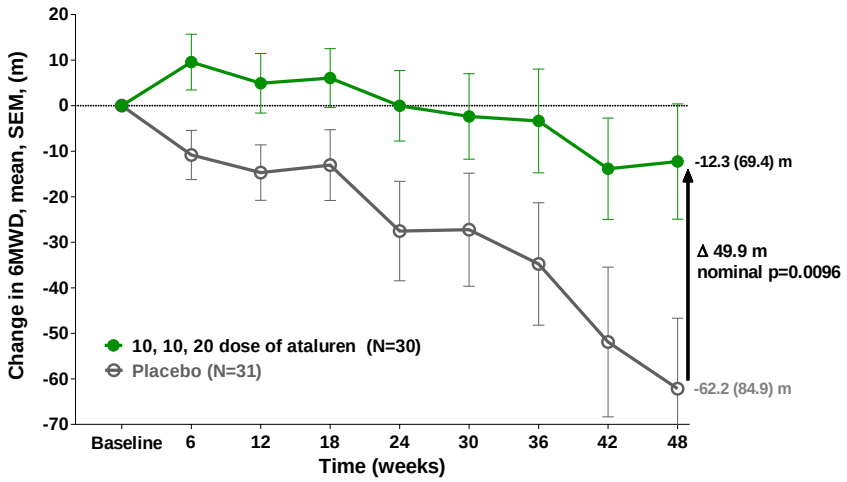
PTC implemented the following enrollment criteria for the confirmatory Phase III trial based on the findings from a *post hoc* analysis of the Phase IIb trial.

- Patients must be between the ages of seven and 16
- Patients must have a baseline 6MWT performance that is at least 150 meters but no more that 80% of the walk distance predicted for healthy boys matched for age and height
- Patients must have received systemic corticosteroid treatment for a minimum of six months prior to receiving ataluren treatment

We believe the enrollment criteria will benefit PTC in demonstrating the clinical benefit of ataluren treatment over placebo in the confirmatory Phase III trial. Data from natural history studies have suggested that the group of patients being targeted for the trial – DMD patients older than seven years of age with baseline walking ability below a certain level – are more likely to be in a declining phase in walking ability without medical intervention and as a result, it will be easier for PTC to distinguish ataluren-induced maintenance of walking ability from the mere lack of deterioration in younger and healthier patients. Additionally, required corticosteroid use will further help PTC achieve a more uniform group of patients who are more likely to have stable performance, so that the variance in data collected in the trial can be reduced.

PTC's *post hoc*, retrospective subgroup analysis of the Phase IIb clinical trial data included only patients who would qualify for the confirmatory Phase III clinical trial based on the modified inclusion criteria. The subgroup analysis demonstrated an improved clinical benefit with a p value much above the threshold for statistical significance from low-dose ataluren treatment as compared to placebo.

Exhibit 25. A More Significant Clinical Benefit In Phase III Target Patient Population



Source: PTC Therapeutics, Inc.

The ongoing Phase III clinical trial of Prosensa/GSK's drisapersen has similar patient enrollment criteria and an assumed standard deviation comparable to those of the completed Phase IIb clinical trial of ataluren. However, an important difference between the two trials is the patient number enrolled in each treatment cohort: drisapersen's Phase III trial has only two treatment cohorts, each enrolling approximately 93 patients whereas ataluren's Phase IIb trial enrolled 57 patients in each of the active treatment cohorts and the placebo cohort. The larger patient numbers in drisapersen's Phase III trial may help in achieving statistical significance in a pre-specified endpoint analysis.

Exhibit 26. Patient Enrollment Comparison Across DMD Trials

Drug	Stage	Number of Patient	Age	Baseline 6MWD	Assumed Common Standard Deviation
Ataluren	Comfirmatory Phase III	220	≥7	150 meters to 80% of matched healthy peers	72 meters
Ataluren	Phase IIb	174	≥5	≥75 meters	50 meters (actual 72 & 90 meters)
Eteplirsen	Phase IIb	12	7-13	280-440 meters*	NA
Drisapersen	Phase III	186	≥5	≥75 meters	55 meters

* This is the initial enrollment criteria but the analysis on the 6MWD was conducted in the mITT group of ten patients

Source: PTC Therapeutics, Inc., Sarepta Therapeutics, Inc., GSK & Cowen and Company

In contrast, eteplirsen's Phase IIb trial has similar patient enrollment criteria to those of ataluren's confirmatory Phase III clinical trial. Even with a significantly smaller sample size of only ten patients in the modified intent-to-treat (mITT) population, which in theory would give rise to a large variance, the standard error from the following company data presentation is approximately 15 meters, which would translate into a standard deviation of approximately 50 meters.

PTC has increased the size of the confirmatory Phase III clinical trial to enroll approximately 110 patients in each of the two cohorts, thereby improving the possibility of reaching statistical significance in a primary endpoint analysis. The sample size is based on an assumed standard deviation of 72 meters and the trial is powered at 85% to detect an improvement of 30 meters in the 6MWD.

The confirmatory Phase III clinical trial will employ the same rank test for statistical analysis as the *post hoc* analysis of the Phase IIb clinical trial. Notably, PTC has had discussions with the FDA about the trial design and the agency does not require a specific type of statistical analysis, provided that the analysis is pre-specified. In summary, we believe the design of the confirmatory Phase III clinical trial for ataluren bodes well for PTC and we are optimistic that the confirmatory trial should demonstrate a clinical benefit of approximately 30 meters with ataluren treatment.

Ataluren Has A Favorable Safety Profile

Ataluren has demonstrated a strong safety profile to date in over 200 patients. In the Phase IIb clinical trial, both doses of ataluren were well tolerated by patients, with most treatment emergent adverse events being mild to moderate in severity and no discontinuations. The incidence of adverse events was comparable in the ataluren cohorts as in placebo cohort. The most common adverse events from all three cohorts were: vomiting (46.6%), headache (29.3%), diarrhea (24.1%), nasopharyngitis (20.7%), fever (19.0%), cough (19.0%) and upper abdominal pain (17.8%).

Exhibit 27. Ataluren Is Safe And Well Tolerated In Phase IIb Clinical Trial In nmDMD

Characteristic	Placebo N=57	Low-dose N=57	High-dose N=60
Adverse events (AEs) by worst severity*			
Grade 1 (mild)	37%	28%	33%
Grade 2 (moderate)	46%	54%	45%
Grade 3 (severe)	16%	14%	17%
Grade 4 (life-threatening)	0%	0%	0%
AEs by relatedness			
Unrelated	25%	14%	18%
Unlikely	28%	30%	22%
Possible	35%	44%	48%
Probable	11%	9%	7%
Discontinuations due to AE	0%	0%	0%
Serious AEs**	9%	7%	5%

* Grading by Common Terminology Criteria for Adverse Events (CTCAE)
** Serious AEs were those requiring hospitalization

Source: PTC Therapeutics, Inc.

Exhibit 28. Comparable Adverse Event Incidences Between Ataluren And Placebo

Adverse Event	Placebo N=57	Low Dose N=57	High Dose N=60
Vomiting	39%	56%	45%
Headache	25%	39%	25%
Diarrhea	25%	19%	28%
Nasopharyngitis	23%	23%	17%
Pyrexia	21%	25%	12%
Cough	19%	16%	22%
Abdominal pain upper	16%	16%	22%
URT infection	18%	16%	18%
Fall	12%	19%	10%
Nausea	12%	14%	17%
Abdominal pain	7%	12%	17%
Procedural pain	12%	10%	13%
Pain in extremity	11%	12%	13%
Back pain	9%	16%	10%
Influenza	14%	11%	12%

Source: PTC Therapeutics, Inc.

There were a few adverse events that occurred in more than 10% of the patients in each cohort and demonstrated numerically higher incidences in the ataluren cohorts as compared to the placebo cohort, such as vomiting, nausea, abdominal pain and pain in the extremities. However, they are all commonly observed in clinical trials and none should be considered serious. We believe that the highly favorable safety profile of ataluren is a significant plus for PTC, given that decisions on regulatory approvals will be based on the risk-to-benefit ratio. Even for such a life threatening indication as DMD, a safe drug is always desirable. PTC is conducting long-term extension studies in patients who have completed the previous clinical trials. Long-term safety and efficacy results from these trials will add to the strength of the complete data package that PTC will submit in future regulatory filings.

Conditional Approval In The EU

In October 2012, PTC submitted a marketing authorization application (MAA) to the EMA for conditional approval of ataluren for the treatment of nmDMA. In March 2013, PTC received an initial response from the EMA, commonly referred to as the day 120 list of questions which is a list of questions that must be addressed. The EMA's comments focused on the limited evidence of efficacy from the Phase IIb clinical trial and the uncertainties about the effective dose of ataluren. PTC is in the process of preparing responses to the major objections that the EMA raised and the company expects to submit the responses in July 2013. We are taking a conservative approach by not including the conditional approval in the EU in our revenue buildup model due to the large regulatory uncertainty and instead we treat a positive decision from the EMA as upside potential to the PTC model, which in our opinion already represents an attractive investment opportunity even without a conditional approval in the EU.

Exhibit 29. Clinical Development History Of Ataluren For nmDMD

Status	Study	Phase	Design	Location	Total Patients Enrolled
Completed / Ended	nmDMD-004	Phase IIa	Open label	U.S.	38
	nmDMD-004e	Phase IIa extension	Open label	U.S.	36 (from nmDMD-004)
	nmDMD-008	Phase IIa	Open label	U.S.	6
	nmDMD-007	Phase IIb	Randomized, double-blind, placebo controlled	U.S., Canada, EU Israel, Australia	174
Ongoing	nmDMD-007e	Phase IIb extension	Open label	Same as nmDMD-007	173 (from nmDMD-007)
	nmDMD-016	Phase III continuation	Open label	U.S.	Up to 122 (from nmDMD-004 or nmDMD-007)
	nmDMD-019	Phase III continuation	Open label	Canada, EU Israel, Australia	Up to 96 (nmDMD-007)
	nmDMD-020	**Confirmatory Phase III**	**Randomized, double-blind, placebo controlled**	**North America, South America, Europe, Israel, Australia**	**Approximately 220**

Source: Cowen and Company

Genzyme Collaboration

In 2008, PTC and Genzyme entered into an exclusive worldwide collaboration agreement for the development of ataluren for the treatment of nmDMD. Under the agreement, PTC would commercialize ataluren in the U.S. and Canada while Genzyme obtained the rights for other regions of the world. PTC received an upfront payment of $100 million. In September 2011 following the initial negative results from the Phase IIb clinical trial, PTC and Genzyme restructured the agreement for the development of ataluren in the treatment of nmDMD and PTC regained worldwide commercial development rights to ataluren for nmDMD. Genzyme retained an option to commercialize ataluren in indications other than nmDMD outside the U.S. and Canada. The collaboration was officially terminated in March, 2012, when Genzyme notified PTC of the decision not to exercise the option.

An upfront payment of $100 million is a significant investment that indicated Genzyme's strong confidence in both ataluren's clinical profile and the market potential that the drug will be able to address, in our opinion. The restructuring of the collaboration agreement may have been due to the initial negative readout from the Phase IIb clinical trial but may also have been a strategic decision by Genzyme. Genzyme has a much stronger and more diversified pipeline that targets multiple Orphan indications. Additionally, it is much easier to gain favorable pricing for therapeutics for Orphan diseases in the U.S. than in the other regions of the world. Therefore, Genzyme may have decided to give up the less attractive revenues from outside the U.S. and leave the risk to PTC even though ataluren still has strong potential for success both in and outside the U.S.

Cystic Fibrosis

The second indication that PTC is pursuing with ataluren is cystic fibrosis (CF), a chronic genetic disorder caused by mutations in the *cystic fibrosis transmembrane conductance regulator* (*CFTR*) gene. Over 1,600 mutations, including missense, deletion or insertion, frame shift, splice site, and nonsense mutations have been identified since the discovery of the *CFTR* gene. The mutations cause functional defect or a complete loss of production of the CFTR protein, which is an ion channel located on the apical membrane of epithelial cells that regulates the transport of chloride and sodium ions across the membrane.

Pathophysiology And Epidemiology

According to the Cystic Fibrosis Foundation, CF affects approximately 30,000 children and adults in the U.S. and the worldwide prevalence is approximately 70,000. The disease mainly affects the lung and the digestive system, causing the production of unusually thick and sticky mucus due to the dysfunctional CFTR protein. In the lungs, the mucus clogs the airway, leading to chronic lung infections and progressive lung damage. This is the main cause of disease progression and CF patients typically die from respiratory failure. In the digestive system, the mucus blocks the pathway within the pancreas and prevents secreted enzymes from entering the gastrointestinal track to help with digestion, leading to permanent pancreatic damage and malnutrition. CF is a life threatening disease and in the past patients typically died before school age. With the recent development of therapeutics, the life expectancy of CF patients has been extended to the 30s and beyond. The natural history of CF consists of chronic progression of lung function decline with intermittent episodes of acute worsening of respiratory symptoms that are commonly referred to as “pulmonary exacerbations”.

CF is diagnosed with the sweat test – a higher than normal chloride concentration in the sweat indicates that the person has the disease. Additionally, both prenatal screening and newborn screening can identify CF patients. Today, the majority of diagnoses are through newborn screening and almost all patients are identified during infancy, which allows for early intervention and treatment.

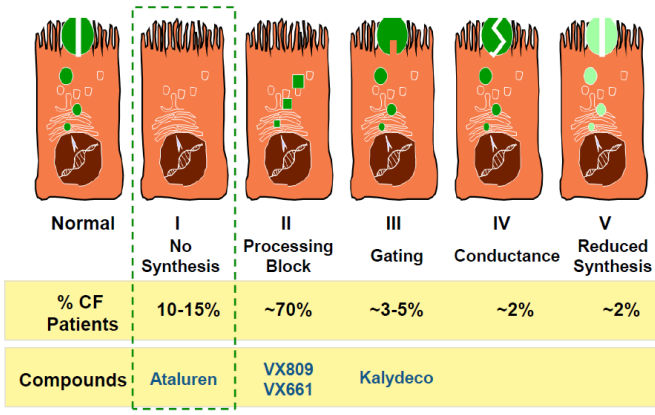
There is no cure available for CF and current treatments, which include the following options, mainly aim to improve symptoms:

- Airway clearance procedures to clear mucus from the lungs
- Inhaled antibiotics such as tobramycin and aztreonam to treat lung infections
- Bronchodilator medicines to help open the airways
- Lung transplantation for severe CF patients

Genetic mutations in the *CFTR* gene that cause CF can be divided into five different classes, from Class I to Class V, based on how severely they affect the production of the CFTR protein and the amount of residual CFTR function on the membrane of the cells. Different *CFTR*

mutations affect different steps during the protein production process. Nonsense mutations that completely block the production of the CFTR protein belong to Class I, which is the most severe type of mutation and represents approximately 10% of CF patients. Class II mutations affect trafficking of CFTR protein and contain the most prevalent mutation F508del. The CFTR protein fails to reach the cell surface and there is little residual protein function maintained. Class III mutations are gating mutations: the CFTR protein is able to reach the cell surface but the ion channel behaves like a locked gate and there is no flow of ions and fluids across the cell membrane. Class IV mutations cause narrowing of the ion channels and Class V mutations affect the mRNA processing step during CFTR protein synthesis. Both Class IV and Class V mutations reduce the amount of functional CFTR protein on the cell surface, leaving some residual CFTR function, but they only affect a small percentage of CF patients.

Exhibit 30. Genetic Mutation Classes For CF



Source: PTC Therapeutics, Inc.

Success Of Kalydeco Bodes Well For Ataluren

Vertex Pharmaceuticals is actively developing novel treatments for CF. Kalydeco, an orally available small molecule "CFTR potentiator", received FDA approval in January 2012 for CF patients age six and older with at least one copy of the G551D mutation in the *CFTR* gene. G551D mutation is the most common form of the Class III gating mutations and in affected CF patients, the CFTR protein is able to traffic to the correct location on the surface of the epithelial cells but the ion channel gate is locked. Kalydeco was the first drug to address the underlying cause of CF by increasing the probability of opening of the CFTR channel.

Vertex filed an NDA for Kalydeco in November 2011 and received the official approval in January 2012, more than two months ahead of the PDUFA date. The accelerated timeline indicated that the FDA recognizes the unmet medical need for efficacious and safe CF therapies. Moreover, the FDA has granted Breakthrough Therapy Designation to the Kalydeco monotherapy program for additional indications as well as a combination regimen of Kalydeco with another investigational compound VX-809 for patients with a different type of mutation.

The two programs were the first to receive this designation for accelerated clinical development.

Kalydeco achieved rapid penetration in the U.S. after FDA approval. Vertex booked net product revenues of $171.6MM from Kalydeco sales in 2012 and management estimates that most eligible patients in the U.S. have initiated and are receiving Kalydeco treatment. On the company's 4Q12 earnings conference call, management guided to Kalydeco revenue of $280MM to $320MM in 2013, with all growth above 3Q12's quarterly run rate of approximately $50MM per quarter to be from Europe. The target CF patient population for Kalydeco accounts for approximately 3% to 5% of the entire CF patient population whereas approximately 10% of the all CF patients will be eligible for and will likely benefit from ataluren treatment. Therefore, should PTC be able to demonstrate a strong clinical profile for ataluren in the treatment of CF to receive FDA approval for this indication, the company will have a sizable market to penetrate resulting in a strong boost to PTC's top line.

Clinical Trial History In nmCF

Phase II Open Label Clinical Trials

In 2006, PTC completed two open label Phase II clinical trials that evaluated ataluren for the treatment of nmCF in a total of 47 adult patients. The first trial was conducted at one clinical site in Israel and the second trial was conducted at four clinical sites in the U.S. In 2008, PTC further completed a third open-label Phase II clinical trial in France and Belgium that evaluated ataluren in a total of 30 pediatric and adolescent nmCF patients between the ages of six and 18 years.

All three trials had similar designs and included two treatment cycles, each containing a 28-day treatment period, which further consisted of two weeks of continuous ataluren treatment and a two-week follow-up period without treatment. During the first cycle, patients received ataluren at doses of 4mg/kg, 4mg/kg, and 8mg/kg in the morning, at midday and in the evening, respectively, for a total daily dose of 16mg/kg. During the second cycle, patients received 10mg/kg, 10mg/kg and 20mg/kg on the same schedule for a total daily dose of 40mg/kg. Patients were evaluated at the beginning and end of each two-week treatment period and the two-week follow-up period in each cycle. The primary endpoint of the trials was the change in CFTR-mediated chloride conductance in respiratory cells, as measured with nasal transepithelial potential difference (TEPD, the voltage across an epithelium), between the beginning and the end of treatment.

The adult trial in Israel and the pediatric trial in France and Belgium demonstrated a statistically significant improvement at the end of the ataluren treatment period in both the mean total chloride conductance and the percentage of patients with a total chloride conductance response of at least a -5.0mV improvement, which is normally considered clinically meaningful. However, the U.S. adult trial failed to demonstrate any improvement in the mean total chloride conductance.

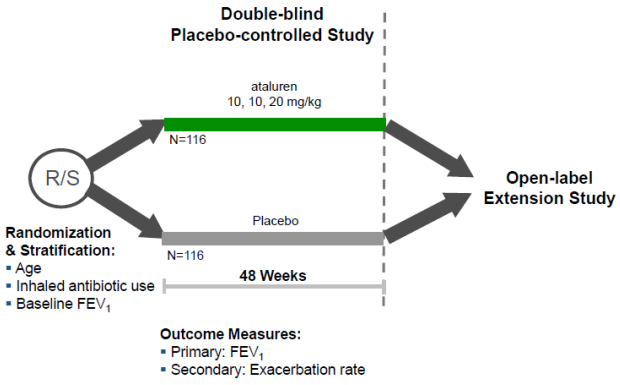
Ataluren was safe and well tolerated in the Phase II clinical trials. Only one serious adverse event, an episode of distal intestinal obstruction syndrome (DIOS) which is a well-known complication of CF patients, was deemed by the investigator to be possibly related to active treatment. The patient had experienced DIOS in the past and the syndrome resolved completely after treatment was stopped. Adverse events that may have been treatment-related were generally mild in severity.

Phase III Clinical Trial

In December 2008, PTC initiated a randomized, double-blind, placebo controlled international Phase III clinical trial to evaluate ataluren for the treatment of nmCF; results were announced in June 2012. The trial enrolled a total of 238 patients who were at least six years of age and had a confirmed nonsense mutation in at least one allele of the *CFTR* gene. The primary endpoint of the trial was relative change in forced expiratory volume in one second as a percentage of predicted (%FEV_1), a key measure commonly used to monitor lung function and to assess disease severity in CF and other lung diseases. Secondary endpoints included pulmonary exacerbation frequency, patient compliance with drug administration and the pharmacokinetics of ataluren.

Patients were required to have a %FEV_1 of between 40% and 90% to be enrolled in the Phase III clinical trial and they were randomized in a 1:1 ratio to receive either ataluren at 10mg/kg in the morning, 10mg/kg at midday, and 20mg/kg in the evening, or matching placebo. The treatment duration was 48 weeks and patients made clinic visits every eight weeks to have their %FEV_1 measured. The pre-specified trial protocol defined the intent-to-treat (ITT) patient population as those who were randomized and had %FEV_1 data available at baseline and at least one post-baseline visit. The final ITT population consisted of 116 patients from the ataluren treatment arm and 116 patients from the placebo arm.

Exhibit 31. Design Of The Phase III Clinical Trial In CF



Source: PTC Therapeutics, Inc.

The Phase III clinical trial was designed to detect a relative change in %FEV_1 of at least 6% or greater in the ataluren cohort as compared to the placebo cohort from baseline to the end of 48 weeks of treatment. The actual data demonstrated a 3.0% difference (a 2.5% decrease in the

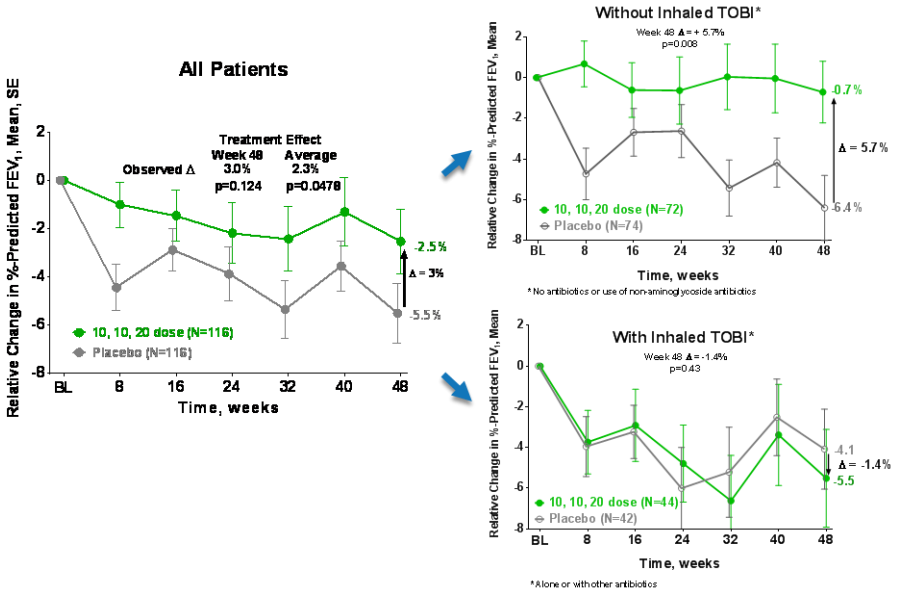
ataluren cohort as compared to a decrease of 5.5% in the placebo cohort) from baseline to end of treatment at week 48, which failed to achieve statistical significance (p=0.124). The analysis of absolute change in $\%FEV_1$ at week 48 failed to achieve statistical significance as well (a 1.3% decrease in the ataluren cohort as compared to a decrease of 3.1% in the placebo cohort, p=0.136).

An alternative analysis, based on the average treatment effect across all post-baseline visits, demonstrated a statistical significance in the relative change in $\%FEV_1$ between the ataluren and the placebo cohorts (a 1.8% decrease in the ataluren cohort as compared to a decrease of 4.3% in the placebo cohort, p=0.0478).

Subgroup Analysis Demonstrates Clinical Benefit In Non-TOBI Patients

PTC conducted a subgroup analysis and discovered that chronic use of inhaled antibiotics, particularly tobramycin (TOBI), had a substantial impact on the treatment effect of ataluren. In the patients who were not receiving chronic inhaled tobramycin, ataluren treatment demonstrated a difference of 5.7% in the mean relative change in $\%FEV_1$ from baseline to week 48 (nominal p=0.008). This is in line with the targeted treatment effect that the Phase III trial was initially designed to detect. In contrast, no benefit from ataluren treatment was detected in patients who were receiving chronic inhaled tobramycin. Two other inhaled antibiotics used by patients in the Phase III clinical trial, colistin and aztreonam, had no impact on the treatment effect of ataluren.

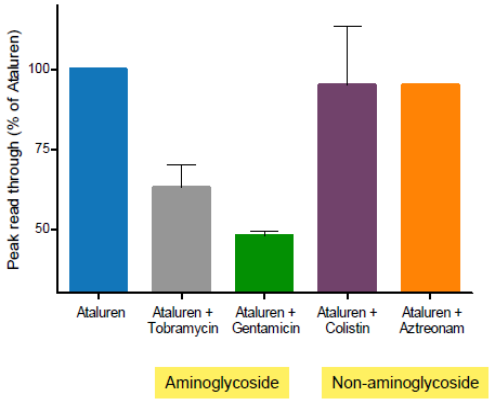
Exhibit 32. Ataluren Demonstrates Clinical Benefit In Non-TOBI Patients



Source: PTC Therapeutics, Inc.

Tobramycin is an aminoglycoside and as we have discussed in previous sections of this report, aminoglycosides are well known for their binding to ribosomes to modulate genetic translational machinery. Therefore, it is likely that tobramycin is competing with ataluren for the same binding site on the ribosome, thereby interfering with ataluren's activity. This hypothesis was supported by a functional cell-based translation assay conducted by PTC, which demonstrated that exposure to tobramycin or gentamicin reduced ataluren-induced premature stop codon readthrough in cells. However, neither colistin nor aztreonam demonstrated such a negative effect.

Exhibit 33. Only Aminoglycosides Have A Negative Impact On Ataluren Activity



Source: PTC Therapeutics, Inc.

The Phase III clinical trial evaluated pulmonary exacerbation rates in patients as the secondary endpoint. The same negative effect from use of inhaled tobramycin was observed again, with a statistically significant clinical benefit detected only in patients not receiving TOBI (p=0.005) but not in the entire patient population when observed on an ITT basis (p=0.099).

Exhibit 34. Ataluren Reduces The Pulmonary Exacerbation Rate In Non-TOBI Patients

	% decrease in pulmonary exacerbation*
Overall population (N=232)	23%
	p=0.0992
Non-TOBI patients (N=146)	41%
	nominal p=0.005

*** Modified Fuchs definition**

Source: PTC Therapeutics, Inc.

The tertiary endpoints in the Phase III clinical trial included nasal TEPD and sweat chloride concentration, two tests commonly used in the diagnosis of CF and in evaluating the severity of the disease, and other parameters such as hourly cough rate, respiratory domain score from

a questionnaire, inflammatory markers and lung computed tomography. None of the tertiary endpoints demonstrated a statistically significant difference between ataluren and placebo.

Ataluren continued to demonstrate a strong safety profile in the Phase III clinical trial, with rates of adverse events comparable between the ataluren treatment cohort and the placebo cohort. Most serious adverse events were pulmonary exacerbation from CF that was not deemed related to study drug and most treatment emergent adverse events were mild to moderate in severity. CF pulmonary exacerbation was also the most frequent adverse event (78.2% overall), followed by cough (25.6%) and viral upper respiratory tract infection (21.0%) which are typical of CF as well. Adverse events that occurred in more than 10% of the patients in each cohort and demonstrated numerically higher incidences in the ataluren cohort as compared to the placebo cohort included headache, abdominal pain, sinusitis, and vomiting. A total of 11 patients, eight from the ataluren cohort and three from the placebo cohort, discontinued treatment due to adverse events.

Exhibit 35. Strong Safety And Tolerability Of Ataluren In nmCF Phase III Clinical Trial

	Treatment arm		
Parameter	Placebo N=118	Ataluren N=120	All patients N=238
Patients with ≥1 adverse event	115 (97.5%)	118 (98.3%)	233 (97.9%)
Adverse events by severity			
Grade 1 (mild)	20 (16.9%)	18 (15.0%)	38 (16.0%)
Grade 2 (moderate)	65 (55.1%)	81 (67.5%)	146 (61.3%)
Grade 3 (severe)	30 (25.4%)	19 (15.8%)	49 (20.6%)
Grade 4 (life-threatening)	—	—	—
Adverse events by relatedness			
Unrelated	42 (35.6%)	30 (25.0%)	72 (30.3%)
Unlikely	31 (26.3%)	39 (32.5%)	70 (29.4%)
Possible	35 (29.7%)	34 (28.3%)	69 (29.0%)
Probable	7 (5.9%)	15 (12.5%)	22 (9.2%)
Discontinuations due to adverse events	3 (2.5%)	8 (6.7%)	11 (4.6%)
Serious adverse events	48 (40.7%)	45 (37.5%)	93 (39.1%)
Deaths	—	—	—

Source: PTC Therapeutics, Inc.

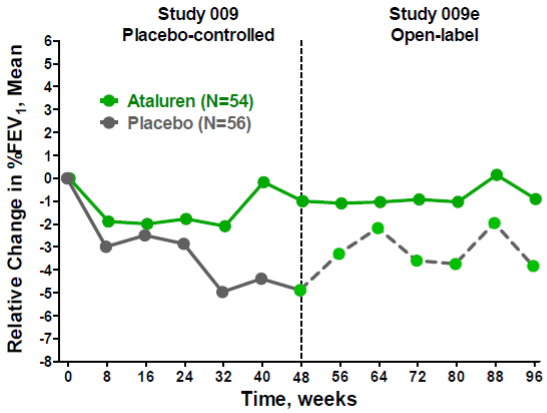
Ataluren treatment induced a higher rate of treatment-emergent renal adverse events, with 15 ataluren-treated patients experiencing at least one event as compared to four placebo-treated patients. Creatinine elevations, an important indicator of impaired renal health, were observed with a higher incidence in the ataluren cohort as compared to the placebo cohort, although most of the events were mild and transient. This issue resolved after concomitant use of ataluren and potentially nephrotoxic antibiotics such as aminoglycosides or vancomycin was discontinued. Therefore, we believe that this concern can be sufficiently managed with adequate physician and patient education.

Stabilized Lung Function Observed In Open Label Extension Study

The ongoing open-label extension study enrolled 191 patients who completed the double-blind phase of the Phase III clinical trial and is evaluating the safety and efficacy of long-term

administration of ataluren in CF patients. Patients will receive ataluren for a 96-week treatment period and will make clinic visits every eight weeks to receive assessments on their pulmonary function and pulmonary exacerbations. Data from patients who have completed the 96-week treatment period suggest that long-term ataluren treatment maintained pulmonary function in the patients who were enrolled in the active treatment cohort in the Phase III clinical trial and also slightly reverse the pulmonary exacerbation in patients who were enrolled in the placebo cohort and then switched over at the beginning of the extension study. Ataluren demonstrated a similar safety profile as observed in the double-blind phase of the Phase III clinical trial.

Exhibit 36. Long-Term Ataluren Administration Stabilizes Pulmonary Function



Data current as of Sept 2012; relative change in %-predicted FEV_1 in 110 patients through Week 96

Source: PTC Therapeutics, Inc.

Conditional Filing In The EU And Planned Confirmatory Phase III Clinical Trial

PTC has received scientific advice from the EMA on the possibility of submitting an MAA for the conditional approval of ataluren for the treatment of nmCF as well as regarding the protocol design of the post-approval confirmatory Phase III clinical trial. PTC plans to submit the MAA in 2H13. We are taking a conservative approach and have not included an EU conditional approval for nmCF in our financial model.

PTC expects to initiate the confirmatory Phase III clinical trial of ataluren for the treatment of nmCF in 2H13 and to dose the first patient in 1H14. PTC is currently in discussions with the FDA regarding the clinical trial design of the confirmatory Phase III clinical trial for nmCF and the company's goal is to achieve consensus between the FDA and the EMA so that a single confirmatory Phase III trial will be sufficient to support regulatory filings for full approvals in both the U.S. and the EU. We believe the trial design has not been finalized as the company has not provided specific guidance except that patients receiving TOBI will be excluded but other inhaled non-aminoglycoside antibiotics will be available for enrolled nmCF patients.

We believe PTC will aim to choose the optimal patient population to demonstrate the greatest magnitude of clinical benefit from ataluren treatment in the nmCF confirmatory Phase III clinical trial as the company did in the nmDMD trial. The experience and the lessons from the previous Phase III clinical trial will provide PTC with valuable information with regard to trial design. Additionally, the ongoing discussions with both the FDA and the EMA should provide PTC with sufficient input from the regulatory agencies. We are optimistic that the statistically significant improvement in lung function as measured with $\%FEV_1$ in nmCF patients not receiving TOBI will likely be replicated in the confirmatory Phase III clinical trial.

Exhibit 37. Clinical Development History Of Ataluren For nmCF

Status	Study	Phase	Design	Location	Total Patients Enrolled
Completed / Ended	nmCF-003	Phase II	Open label	U.S.	24
	nmCF-005	Phase II	Open label	Israel	23
	nmCF-005e	Phase IIa extension	Open label	Israel	19 (from nmCF-005)
	nmCF-006	Phase IIa	Open label	Belgium, France	30
	nmCF-009	Phase III	Randomized, double-blind, placebo controlled	North America, Europe, Israel	238
Ongoing	nmCF-009e	Phase III extension	Open label	North America, Europe, Israel	191 (from nmCF-009)
Planned	**nmCF-021**	**Confirmatory Phase III**	**Randomized, double-blind, placebo controlled**	**Global**	**Approximately 210**

Source: PTC Therapeutics, Inc.

Competitive Landscape: There Is No Direct Competition In Either DMD Or CF

As we have discussed in the previous section of this report, ataluren does not compete with eteplirsen or drisapersen for DMD patients and is the only therapeutic currently under clinical development for nmDMD.

Similarly, ataluren does not have direct competitors for CF patients. Vertex is conducting several additional studies for Kalydeco monotherapy in order to broaden its indication beyond the G551D population. These studies include a pediatric study being conducted in children between the ages of two and five with gating mutations and studies in CF patients with other types of gating mutations. Additionally, Vertex is developing VX-809 and VX-661, two "CFTR correctors" that help the CFTR protein reach the surface of epithelial cells, both as monotherapy and in combination therapy with Kalydeco to address a broader CF patient

population. None of the ongoing Vertex programs are targeting CF patients with nonsense mutations in the *CFTR* gene. The ultimate goal of Vertex is to cover up to 90% of CF patients with the company's therapeutic regimens. This ambitious plan should not affect ataluren, in our opinion, since the Vertex approaches do not address CF patients with nonsense mutations, that don't produce any CFTR protein. These patients should be the remaining 10% who will be eligible for ataluren treatment.

There have been continued efforts, both from PTC and from other groups, to identify non-aminoglycoside small molecule compounds that promote readthrough of premature stop codons. PTC has identified a second generation compound that likely has a higher potency in inducing premature stop codon readthrough. We believe that the expertise and experience that PTC continues to garner from ataluren will significantly benefit the clinical development of the second generation compound. In the meantime, other research groups have also discovered potential candidates with similar activity but none are close to entering the clinic, so they do not pose a meaningful threat to the potential market share that ataluren will likely achieve.

Commercialization Is Less Challenging

A focus on Orphan indications makes it possible for PTC to commercialize ataluren independently both in the U.S. and potentially in the EU as well. PTC anticipates that a small and focused specialty sales force will be sufficient to support the commercialization of ataluren for both nmDMD and nmCF.

Vertex has established a proprietary commercial organization to support the sale of Kalydeco in both the U.S. and other markets. The company's U.S. field-based CF commercialization team includes approximately 15 specialists. Since both DMD and CF are rare diseases, it is reasonable to estimate that a relatively small number of specialty physicians are treating the majority of the patients. Therefore, PTC should also be able to cover the entire treating communities for both DMD and CF with a small sales force.

Limitations Of Ataluren

We believe that ataluren is a highly promising candidate that will likely provide patients suffering from genetic disorders caused by nonsense mutations with a safe and efficacious option of treatment. However, ataluren also has the following limitations and they are mainly related to the drug's mechanism of action.

Varied Efficacy Depending On Stop Codon

A major concern with premature stop codon read-through is the variation in the efficiency for different stop codons. In the genetic code, there are three different combinations of nucleotides for a stop codon and each has a different efficiency for read-though. Studies conducted by PTC demonstrated that the readthrough efficiency of ataluren is the highest for UGA, the stop codon used in the initial screening for the compound, followed by UAG and UAA. Therefore,

the treatment effects will likely be different among patients depending on the type of premature stop codon that each patient has. Additionally, the efficiency of readthrough is also dependent on the adjacent sequence context. The sequences before and after the premature stop codon, particularly the immediate downstream nucleotide following the premature stop codon (+4 position), are important in determining the readthrough efficiency.

Moreover, the insertion of an amino acid to replace the premature stop codon can be random and therefore, the process will also create significant variability. Although the chances are low, the possibility still remains that a single amino acid may bring dramatic changes to the characteristics of a protein such as its structure and function. As a result, there is no absolute guarantee that the newly produced "full-length" protein will have the same physiological function of the normal protein.

No Effect On The NMD Pathway

Nonsense transcripts that contain premature stop codons are susceptible to rapid degradation by the NMD pathway. Down regulation of the NMD pathway, by increasing the amount of nonsense transcripts, has been demonstrated to enhance the physiological function of the newly generated full-length proteins in response to gentamicin treatment. Therefore, the NMD pathway may be important for readthrough efficiency and in some genetic disorders, *BOTH* inhibition of the NMD pathway *AND* translational readthrough may be required to achieve clinically meaningful treatment benefits. Ataluren promotes premature stop codon readthrough by altering the termination efficiency during protein translation but does not affect the NMD pathway. As a result, the mRNA containing nonsense mutations will still remain susceptible to rapid degradation and this may significantly limit the amount of substrate available for ataluren's therapeutic effects. We believe that more optimal treatment effects may be achieved using approaches that combine ataluren with certain therapies that inhibit the NMD pathway.

Lack Of Convincing Dystrophin Production Data In The Phase IIb Clinical Trial

DMD is caused by disruption of proper dystrophin production and most therapeutic approaches in development aim to restore dystrophin protein production. PTC demonstrated dystrophin production in the Phase IIa clinical trial but similar data is lacking from the completed Phase IIb clinical trial. Moreover, dystrophin expression is not included as one of the endpoints of the ongoing confirmatory Phase III clinical trial, whereas Sarepta Therapeutics and Prosensa/GSK, which are developing exon-skipping technology based therapeutics for the treatment of a different sub-population of DMD patients, are both evaluating dystrophin protein production in their clinical trials.

We believe that it is highly challenging to measure the level of dystrophin production levels accurately with muscle tissue biopsies and there may not be a direct correlation between dystrophin production levels and clinical benefit as measured with the well-established 6MWT. However, should PTC be able to provide clear and convincing qualitative data of dystrophin

production, the entire data package would be much stronger and both the FDA and investors would be better convinced, in our opinion.

CF Trial Data, What Is A Clinically Meaningful Improvement?

Physicians believe that CF patients on average lose one percentage change in $\%FEV_1$ per year. Therefore, an improvement of 5.7% that ataluren demonstrated in non-TOBI patients would be equivalent to delaying disease progression by approximately six years.

However, there is inherent variability in $\%FEV_1$ measures within individual patients due to day-to-day fluctuation in lung function and potential measurement error. As a result, although there is a correlation between $\%FEV_1$ and disease progression in a large population of patients on average over a number of years, measuring $\%FEV_1$ in any single patient at any given time point can be imprecise.

In addition to the significant variation in $\%FEV_1$ measurement, it is possible that the larger deterioration of lung function in non-TOBI patients who received placebo in PTC's completed Phase III clinical trial as compared to the entire placebo-treated patient group might have been partially due to a higher rate of infections caused by lack of effective antibiotic treatment.

Antibiotic Use In CF Patients

Antibiotics are typically used to treat pulmonary exacerbations and the choices are driven by *Pseudomonas aeruginosa*, the most common strain of pathogen identified in CF patients. *Pseudomonas aeruginosa* colonization occurs in approximately 90% of CF patients at some point during their lives. Aminoglycosides are routinely used for the treatment of CF patients due to their strong activity against *Pseudomonas aeruginosa*. According to the Cystic Fibrosis Foundation, TOBI is one of the most widely used treatments for people suffering from CF. However, data from PTC's completed Phase III clinical trial in nmCF suggest that patients will not benefit from ataluren treatment while remaining on TOBI and the planned confirmatory Phase III study is excluding patients receiving TOBI. The interference of ataluren's mechanism of action by TOBI will limit the target patient population for ataluren even though non-aminoglycoside antibiotics, such as inhaled colistin or aztreonam, are available since there may be patients who are allergic or resistant to these alternative antibiotics.

In summary, ataluren has limitations but we do not believe they will significantly affect either the outcome of the confirmatory Phase III clinical trials or future commercialization efforts.

Additional Programs

Second Generation Readthrough Compounds Aim At Increased Efficacy

PTC is actively engaged in the identification of additional compounds with increased activity in nonsense mutation suppression. The aim is to improve the readthrough activity at all three stop codons, to achieve a more desirable pharmacodynamic profile so that twice-daily or even once-daily dosing can become a possibility, and to increase tissue exposure while maintaining a strong safety profile. The company has tested several therapeutic candidates in multiple disease models and has observed positive results, suggesting an improved clinical profile as compared to ataluren.

Additionally, PTC is screening for compounds that can modulate the NMD pathway to stabilize mRNA molecules that contain premature stop codons. As we have discussed, ataluren does not have this function and therefore its activity is limited by the amount of premature stop codon-containing mRNA. By combining modulation at both the NMD pathway level and protein translation level, PTC should be able to achieve higher efficacy in inducing the production of functional full length proteins.

SMA Program Is Next Up To Bat

Spinal Muscular Atrophy (SMA) is an autosomal recessive neuromuscular disorder that affects approximately one in every 10,000 newborns. SMA is caused by mutations in the *SMN1* gene that lead to reduced levels or complete elimination of survival motor neuron (SMN) protein production. As a result, motor neurons in the anterior horn of the spinal cord degenerate gradually and progressive atrophy occurs in motor muscles. No effective treatment is available for SMA and the disease is a leading cause of death among infants and toddlers. Due to the low disease prevalence, therapeutics for SMA should be eligible for Orphan Drug Status in both the U.S. and the EU.

PTC initially entered into a research and development collaboration agreement with the SMA Foundation in June 2006 to utilize the company's proprietary Gene Expression Modulation by Small-molecules (GEMS) technology to identify and develop novel small-molecule compounds for the treatment of SMA. The aim is to modulate the translation process to increase SMN1 protein levels. The first round of funding provided PTC with $1.6 million and the company later received another $1.6 million upon completing certain milestones. In May 2009, PTC and the SMA Foundation further expanded the research collaboration with an additional round of funding of $8.5 million, bringing total funding to $13.3 million.

In November 2011, PTC and the SMA Foundation announced a licensing agreement with Roche, which obtained an exclusive worldwide license to PTC's SMA program that includes three compounds in preclinical development and potential back-up compounds.

PTC received an upfront payment of $30 million and will be entitled to $460 million in future payments upon successful completion of certain development and commercialization milestones, as well as up to double-digit royalties on commercial sales. The SMA Foundation will remain active in the collaboration.

The current SMA program has been developed by PTC utilizing a different scientific approach than GEMS, called alternative splicing. In human and animal cells, pre-mRNA is transcribed from DNA in the nucleus and often contains multiple introns. The process of intron removal is called RNA splicing and mature RNA exits the nucleus after splicing to be translated within ribosomes in the cytoplasm. In alternative splicing, different combinations of exons can be connected to form the final mature RNA. Multiple protein isoforms can be produced from one single gene through alternative splicing of the pre-mRNA and may have distinct functions. While alternative splicing contributes to the efficiency in gene expression regulation and creates genetic diversity, it has also been found to be involved in a large proportion of human genetic diseases when abnormal splicing produces aberrant protein products.

SMA has a wide spectrum and the most severe form, Type 1, is caused by deletion mutations in both copies of the *SMN1* gene that completely block protein production. In milder forms of SMA, point mutations convert the *SMN1* gene into the *SMN2* gene, which is located on the same chromosome but in a different region. The *SMN2* gene produces the same protein as SMN but undergoes alternative splicing and as a result, up to 90% of the transcripts produce a truncated protein which is degraded rapidly in the body. Only 10% to 20% of the *SMN2* gene produces functional full-length SMN protein, which allows the neurons to survive.

PTC has identified orally available small molecules that restore the correct splicing pattern of the *SMN2* gene. When administered in SMA model mice, the compounds increase the levels of both *SMN2* mRNA and SMN protein. Treatment with these compounds also resulted in increased survival as much as 800% as compared to control mice, restoration of body weight and prevention of motor neuron loss as well as improved motor function. PTC expects to select a lead development compound in 2H13 for further clinical development.

The continued support from the SMA Foundation and the recent participation of Roche speak to the strength of PTC's SMA program and the company's proprietary technology platforms. Although it is still in early stages of development with three compounds in preclinical studies, we are optimistic that the program will generate promising candidate(s) and that PTC's expertise in DMD will help facilitate the further clinical development of the SMA program as well. We have not included the program in our company valuation matrices again to maintain a conservative approach to valuation.

We believe PTC's alternative splicing technology platform could be a significant value driver for the company. With the ability to include or exclude certain exons to modulate the expression of disease-related genes, PTC should be able to expand the clinical development pipeline to include a substantial number of additional indications.

BMI1 For Aggressive And Drug-Resistant Tumors

In July 2012, PTC announced the selection of PTC596, an experimental drug candidate, for the company's BM1 program for aggressive and drug-resistant tumors. PTC596 is an orally available potent and selective inhibitor of BMI1 protein, which functions in the survival and maintenance of tumor stem cells. By reducing BMI1 protein levels through post-translational modification, PTC596 can potentially reduce the survival and proliferation of tumor stem cells. The identification of the candidate triggered the drawdown of a $2.3 million installment of the Seeding Drug Discovery Award that PTC received from the Wellcome Trust Foundation in June 2010.

Antibacterial Program

In December 2011, PTC announced the receipt of a $5 million Seeding Drug Discovery Award from the Wellcome Trust Foundation for the development of small-molecule drugs for the treatment of infections caused by multidrug-resistant (MDR) Gram-negative bacteria. PTC is actively engaged in lead optimization towards the identification of a development candidate from a novel structural class of molecules, which were established by the company and have potent antibacterial activity against Gram-negative bacteria that are resistant to currently available antibiotics.

Strong Intellectual Property Protection From Proprietary Development

PTC has built a comprehensive patent portfolio surrounding ataluren, which the company identified and developed in house. The issued U.S. patents relating to ataluren's composition of matter will provide protection through 2024. Additionally, an issued U.S. patent relating to the therapeutic method of use of ataluren will not expire until 2027. All of these patents may be eligible for the Hatch-Waxman Act which may allow for patent term extension up to five years beyond the original expiration dates. In Europe, PTC holds two issued European patents relating to dosing and methods of manufacture of ataluren, which provide protection until 2016 and 2027, respectively, and likewise are eligible for potential patent term extension.

Financial Analysis Suggests That Shares Are Undervalued

We determine the value of PTC shares by employing four different methodologies. We first used a discounted earnings model and discount our estimated earnings per share from the first year of meaningful revenue back to 12 months from our current time period after applying a reasonable multiple and discount rate. We assume profitability in 2017, with fully diluted estimated EPS of $1.06. We apply a 30x multiple that is in line with industry average to our 2018 fully diluted EPS estimate of $3.80. Based on the risk associated with clinical development and commercialization – although in our view the commercialization risk is limited given the large unmet medical need due to lack of optimal options for treatment and lack of

competition in the same subpopulations of both DMD and CF patients – we discount back by 30% and arrive at what we believe to be a fair valuation.

Exhibit 38. PTC Therapeutics, Inc. Discounted Earnings Model

2018E EPS	
Diluted	$3.80
PE	30
Discount Years	4.5
Discount Rate	30.0%
Valuation	$35.03

Forward P/E Ratio	Discount Rate 55.0%	50.0%	45.0%	40.0%	35.0%	30.0%	25.0%	20.0%
15x	$ 7.94	$ 9.20	$ 10.71	$ 12.55	$ 14.78	$ 17.51	$ 20.90	$25.11
20x	10.58	12.27	14.29	16.73	19.71	23.35	27.86	33.48
25x	13.23	15.33	17.86	20.91	24.63	29.19	34.83	41.85
30x	15.87	18.40	21.43	25.10	29.56	35.03	41.79	50.22
35x	18.52	21.46	25.00	29.28	34.48	40.87	48.76	58.59
40x	21.16	24.53	28.57	33.46	39.41	46.71	55.72	66.96
45x	23.81	27.60	32.14	37.64	44.34	52.54	62.69	75.33
50x	26.46	30.66	35.72	41.83	49.26	58.38	69.65	83.70
55x	29.10	33.73	39.29	46.01	54.19	64.22	76.62	92.07

Source: Cowen and Company

We then use a discounted cash flow (DCF) model to discount the estimated future cash flow booked by PTC to arrive at the calculated present value of the shares of the company. From our revenue buildup model, we estimate cash flow of $328 million to the company in 2020. We employ an industry standard discount rate of 12% and a perpetual growth rate of -2%.

Exhibit 39. PTC Therapeutics, Inc. Discounted Cash Flow Model

Final year FCF	328
Perpetual Growth Rate	-2.0%
Terminal Value	**2,295**
Discount Factor	0.43
Present Value of Terminal Value	**988**
Present Value of Cash Flows	**179**
Enterprise Value	**1,167**
Add: Net cash	180
Market Value	**1,347**
Fully Diluted Shares Outstanding	25.0
Value per Fully Diluted Share	**$53.89**
Probablity of success	*60%*
Risk Adjusted Value per Fully Diluted Share	**$32.34**

Source: Cowen and Company

We further determine the value of PTC shares using a clinical net present value (NPV) model based on the peak U.S. sales revenue for ataluren in the year of 2024, the last year of the current patent life of ataluren in the U.S. without any patent term extension, in our revenue buildup model. We estimate the market penetration will reach the peak of 70% in the U.S. and 55% in the EU in nmDMD patients. In the same year, we estimate the market penetration in eligible nmCF patients to be 50% in the U.S. and 40% in the EU. Our projected 2024 ataluren revenue will be approximately $582.6 million for nmDMD and 396.7 million for nmCF. We assign a success probability of 60% for ataluren for both indications based on the

demonstrated clinical profile and the late stage of clinical development. We employ 100% for the overall economics based on the projection that PTC will commercialize ataluren independently in both the U.S. and the EU. Taking into account the number of current shares outstanding, we obtain a clinical NPV of $31.87 for alaluren, within which $18.96 comes from the nmDMD program and $12.91 is from the nmCF program.

Exhibit 40. PTC Therapeutics, Inc. Clinical NPV Model

Drug name	Indication	Status	Launch	Success	Peak Sales (US$m)	Economics	Profitability	NPV (US$)
Atularen	DMD	PIII	2016	60%	583	100%	90%	18.96
Atularen	CF	PIII	2017	60%	397	100%	90%	12.91
							Total	31.87

Source: Cowen and Company

Finally, we use a comparable company analysis, which is composed of companies working within a similar therapeutic area as PTC or that are at the same stage of clinical development, namely late-stage clinical trials focusing on a defined therapeutic area. We then compare the mean technology value of the comparable universe ($1361.5 million) to that of PTC ($199.6 million). The comparison demonstrates that shares of PTC are currently trading at a discount of 85% to the mean technology value of the comparable universe.

Exhibit 41. PTC Therapeutics, Inc. Comparative Analysis

Company	Ticker	Enterprise Value ($MM)	Price 25-Jul-13	Shares Out (MM)	Market Cap ($MM)	Cash ($MM)	Debt ($MM)	Cowen Rating
Achillion Pharmaceuticals	ACHN	579.8	$7.21	85.9	619.0	39.4	0.3	1
Acorda Therapeutics	ACOR	1480.1	$37.95	39.8	1511.6	34.7	3.1	1
Synageva BioPharma	GEVA	1250.0	$48.60	26.8	1303.7	53.8	0.0	1
Isis Pharmaceuticals	ISIS	3026.3	$29.27	101.9	2981.9	107.7	152.0	1
Sangamo Biosciences	SGMO	487.1	$10.29	53.8	553.5	66.4	0.0	1
PDL Biopharma	PDLI	1345.6	$8.15	149.1	1215.2	182.2	312.6	2
Sarepta Therapeutics	SRPT	1007.6	$36.90	31.8	1173.9	167.9	1.6	1
Prosensa	RNA	870.6	$29.80	29.0	864.3	0.0	6.3	NA
Mean		**1361.5**			**1277.9**			
PTC Pharmaceuticals	**PTCT**	**199.6**	**$16.14**	**23.8**	**384.1**	**184.5**	**0.0**	**1**

*Coverage at Cowen and Company: ACHN, ACOR & PDLI by Nadeau; SGMO & SRPT by Nash; GEVA & ISIS by Schmidt

Source: Cowen and Company

Exhibit 42. PTC Therapeutics, Inc. Revenue Buildup Model

	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E
Ataluren for Duchenne Muscular Dystrophy (DMD)										
U.S.										
Annual number of births (MM) (-1% annually - economic pressures)	4.0	4.0	3.9	3.9	3.8	3.8	3.8	3.7	3.7	3.7
Incidence of DMD in male infants	1/3,500	1/3,500	1/3,500	1/3,500	1/3,500	1/3,500	1/3,500	1/3,500	1/3,500	1/3,500
Annual incidence of DMD	571	566	560	554	549	543	538	533	527	522
Average life span of DMD patients	25	26	27	28	29	30	31	32	33	34
U.S. prevalence of DMD	14,286	14,709	15,122	15,525	15,918	16,303	16,678	17,043	17,400	17,748
Average age of diagnosis	5	5	5	5	5	5	5	5	5	5
Number of diagnosed DMD patients in the U.S.	11,429	11,880	12,321	12,753	13,174	13,586	13,988	14,380	14,764	15,138
% of DMD patients with nonsense mutations	*13.0%*	*13.0%*	*13.0%*	*13.0%*	*13.0%*	*13.0%*	*13.0%*	*13.0%*	*13.0%*	*13.0%*
Number of U.S. DMD patients amenable to treatment with ataluren	1,486	1,544	1,602	1,658	1,713	1,766	1,818	1,869	1,919	1,968
% Market penetration by ataluren	*10.0%*	*45.0%*	*50.0%*	*55.0%*	*60.0%*	*65.0%*	*70.0%*	*70.0%*	*70.0%*	*70.0%*
Number of U.S. DMD patients receiving ataluren treatment	149	695	801	912	1,028	1,148	1,273	1,309	1,344	1,378
AWP	$125,000	$250,000	$250,000	$250,000	$250,000	$250,000	$250,000	$250,000	$250,000	$250,000
U.S. total ataluren revenue from DMD ($MM)	**18.6**	**173.7**	**200.2**	**228.0**	**256.9**	**287.0**	**318.2**	**327.2**	**335.9**	**344.4**
EU										
EU population (MM)	510.0	511.1	512.2	513.3	514.3	515.4	516.5	517.6	518.7	519.8
EU annual number of birth per 1,000 population	10.3	10.2	10.1	10.0	9.9	9.8	9.7	9.6	9.5	9.4
EU annual number of birth (MM)	5.3	5.2	5.2	5.1	5.1	5.0	5.0	5.0	4.9	4.9
Annual incidence of DMD	750	744	739	733	727	721	716	710	704	699
EU prevalence of DMD	18,761	19,357	19,943	20,518	21,083	21,637	22,182	22,717	23,241	23,757
Number of dianosed DMD patients in EU	15,009	15,634	16,250	16,854	17,448	18,031	18,604	19,167	19,720	20,263
% of DMD patients with nonsense mutations	*13.0%*	*13.0%*	*13.0%*	*13.0%*	*13.0%*	*13.0%*	*13.0%*	*13.0%*	*13.0%*	*13.0%*
Number of EU DMD Patients eligible for ataluren treatment	1,951	2,032	2,112	2,191	2,268	2,344	2,419	2,492	2,564	2,634
% Market penetration by ataluren	*5.0%*	*30.0%*	*35.0%*	*40.0%*	*45.0%*	*50.0%*	*55.0%*	*60.0%*	*60.0%*	*60.0%*
Number of EU DMD patients receiving ataluren treatment	98	610	739	876	1,021	1,172	1,330	1,495	1,538	1,581
AWP	$87,500	$175,000	$175,000	$175,000	$175,000	$175,000	$175,000	$175,000	$175,000	$175,000
EU total ataluren revenue ($MM)	**8.5**	**106.7**	**129.4**	**153.4**	**178.6**	**205.1**	**232.8**	**261.6**	**269.2**	**276.6**
WW total ataluren DMD revenue ($MM)	**27.1**	**280.5**	**329.6**	**381.3**	**435.5**	**492.1**	**551.0**	**588.8**	**605.1**	**621.0**
Ataluren for cystic fibrosis (CF)										
U.S.										
U.S. prevalence of CF		33,295	33,794	34,301	34,816	35,338	35,868	36,406	36,952	37,507
% of CF patients with nonsense mutations		*10.0%*	*10.0%*	*10.0%*	*10.0%*	*10.0%*	*10.0%*	*10.0%*	*10.0%*	*10.0%*
Number of U.S. nmCF patients		3,330	3,379	3,430	3,482	3,534	3,587	3,641	3,695	3,751
% of nmCF patients who can discontinue TOBI		*50.0%*	*50.0%*	*50.0%*	*50.0%*	*50.0%*	*50.0%*	*50.0%*	*50.0%*	*50.0%*
Number of U.S. CF patients amenable to treatment with ataluren		1,665	1,690	1,715	1,741	1,767	1,793	1,820	1,848	1,875
% Market penetration by ataluren		*10.0%*	*25.0%*	*35.0%*	*40.0%*	*45.0%*	*50.0%*	*55.0%*	*60.0%*	*60.0%*
Number of U.S. CF patients receiving ataluren treatment		166	422	600	696	795	897	1,001	1,109	1,125
AWP		$125,000	$250,000	$250,000	$250,000	$250,000	$250,000	$250,000	$250,000	$250,000
U.S. total ataluren revenue from CF ($MM)		**20.8**	**105.6**	**150.1**	**174.1**	**198.8**	**224.2**	**250.3**	**277.1**	**281.3**
EU										
EU prevalence of CF		44,175	44,617	45,063	45,514	45,969	46,428	46,893	47,362	47,835
% of CF patients with nonsense mutations		*10.0%*	*10.0%*	*10.0%*	*10.0%*	*10.0%*	*10.0%*	*10.0%*	*10.0%*	*10.0%*
Number of U.S. nmCF patients		4,418	4,462	4,506	4,551	4,597	4,643	4,689	4,736	4,784
% of nmCF patients who can discontinue TOBI		*50.0%*	*50.0%*	*50.0%*	*50.0%*	*50.0%*	*50.0%*	*50.0%*	*50.0%*	*50.0%*
Number of EU CF patients amenable to treatment with ataluren		2,209	2,231	2,253	2,276	2,298	2,321	2,345	2,368	2,392
% Market penetration by ataluren		*5.0%*	*20.0%*	*30.0%*	*35.0%*	*40.0%*	*45.0%*	*50.0%*	*50.0%*	*50.0%*
Number of U.S. CF patients receiving ataluren treatment		110	446	676	796	919	1,045	1,172	1,184	1,196
AWP		$87,500	$175,000	$175,000	$175,000	$175,000	$175,000	$175,000	$175,000	$175,000
EU total ataluren revenue from CF ($MM)		**9.7**	**78.1**	**118.3**	**139.4**	**160.9**	**182.8**	**205.2**	**207.2**	**209.3**
WW total ataluren CF revenue ($MM)		**30.5**	**183.7**	**268.4**	**313.5**	**359.7**	**407.0**	**455.4**	**484.3**	**490.6**
WW total ataluren sales revenues to PTC ($MM)	**27.1**	**310.9**	**513.3**	**649.7**	**749.0**	**851.8**	**958.0**	**1,044.2**	**1,089.4**	**1,111.6**

Source: Cowen and Company

Exhibit 43. PTC Therapeutics, Inc. Quarterly P&L Model ($MM)

	2011A	2012A	Q1'13A	Q2'13E	Q3'13E	Q4'13E	2013E	Q1'14E	Q2'14E	Q3'14E	Q4'14E	2014E
Revenues												
Ataluren product sales revenue	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Collaboration revenue	99.0	28.8	6.1	5.8	5.5	15.6	33.0	3.8	3.8	3.8	3.8	15.0
Grant revenue	6.5	5.2	1.1	1.1	1.1	1.2	4.5	1.3	1.3	1.3	1.3	5.0
Total revenues and non-cash cancellation revenue	**105.4**	**33.9**	**7.1**	**6.9**	**6.6**	**16.9**	**37.5**	**5.0**	**5.0**	**5.0**	**5.0**	**20.0**
Operating Expenses												
COGS	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Research and development	58.7	46.1	11.3	12.0	11.5	11.7	46.5	12.8	14.0	15.2	16.0	58.0
General and administrative	16.2	14.6	4.5	6.5	6.2	6.8	24.0	6.5	6.7	6.8	7.0	27.0
Sales	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Total Operating Expenses	**74.8**	**60.8**	**15.7**	**18.5**	**17.7**	**18.6**	**70.5**	**19.3**	**20.7**	**22.0**	**23.0**	**85.0**
Income (loss) from operating	**30.6**	**(26.8)**	**(8.6)**	**(11.6)**	**(11.1)**	**(1.7)**	**(33.0)**	**(14.3)**	**(15.7)**	**(17.0)**	**(18.0)**	**(65.0)**
Other non-operating income (loss)												
Interest income (expense), net	(2.4)	(12)	(6.2)	(0.2)	(0.1)	(0.0)	(6.5)	0.0	0.0	0.0	0.0	0.0
Other income (expense), net	0.5	1.8	0.1	0.1	0.1	0.1	0.4	0.1	0.1	0.1	0.2	0.5
Income (loss) from operations before tax benefit	**28.6**	**(26.2)**	**(14.7)**	**(11.7)**	**(11.1)**	**(1.6)**	**(39.1)**	**(14.2)**	**(15.6)**	**(16.9)**	**(17.8)**	**(64.5)**
Tax benefit	2.3	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Deemed dividend	0.0	0.0	(18.2)	0.0	0.0	0.0	(18.2)	0.0	0.0	0.0	0.0	0.0
Net Income (Loss)	**30.9**	**(26.2)**	**(32.9)**	**(11.7)**	**(11.1)**	**(1.6)**	**(57.3)**	**(14.2)**	**(15.6)**	**(16.9)**	**(17.8)**	**(64.5)**
Gain on exchange of convertible perferred stock in connection with recapitalization	0.0	160.0	3.4	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Less beneficial conversion charge	0.0	(0.4)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Net income attributable to common stockholders	**30.9**	**133.3**	**(29.5)**	**(11.7)**	**(11.1)**	**(1.6)**	**(57.3)**	**(14.2)**	**(15.6)**	**(16.9)**	**(17.8)**	**(64.5)**
Tax rate	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*
Income Tax	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Net income (loss) per share - basic	**23.95**	**219.76**	**(2.08)**	**(0.77)**	**(0.44)**	**(0.06)**	**(2.88)**	**(0.56)**	**(0.61)**	**(0.66)**	**(0.68)**	**(2.51)**
Net income (loss) per share - diluted	**4.55**	**42.50**	**(1.83)**	**(0.68)**	**(0.41)**	**(0.06)**	**(2.63)**	**(0.52)**	**(0.57)**	**(0.61)**	**(0.64)**	**(2.34)**
Weighted average common shares outstanding - basic	0.001	0.003	14.2	15.3	25.0	25.2	19.9	25.4	25.6	25.8	26.0	25.7
Weighted average common shares outstanding - diluted	0.006	0.017	16.1	17.2	26.9	27.1	21.8	27.3	27.5	27.7	27.9	27.6

Source: Cowen and Company

Exhibit 44. PTC Therapeutics, Inc. Annual P&L Model ($MM)

	2011A	2012A	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E
Revenues															
Ataluren product sales revenue	0.0	0.0	0.0	0.0	0.0	27.1	202.2	355.0	508.3	604.5	704.3	807.5	914.1	979.3	975.2
Collaboration revenue	99.0	28.8	33.0	15.0	10.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Grant revenue	6.5	5.2	4.5	5.0	5.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Total revenues and non-cash cancellation revenue	**105.4**	**33.9**	**37.5**	**20.0**	**15.0**	**27.1**	**202.2**	**355.0**	**508.3**	**604.5**	**704.3**	**807.5**	**914.1**	**979.3**	**975.2**
Operating Expenses															
COGS	0.0	0.0	0.0	0.0	0.0	4.1	28.3	46.2	61.0	66.5	70.4	80.7	91.4	97.9	97.5
Research and development	58.7	46.1	46.5	58.0	65.0	70.0	65.0	60.0	60.0	60.0	65.0	70.0	75.0	80.0	85.0
General and administrative	16.2	14.6	24.0	27.0	30.0	35.0	37.0	40.0	43.0	45.0	48.0	50.0	52.0	55.0	57.0
Sales	0.0	0.0	0.0	0.0	2.5	12.5	25.0	27.5	30.3	33.3	36.6	40.3	44.3	48.7	53.6
Total Operating Expenses	**74.8**	**60.8**	**70.5**	**85.0**	**97.5**	**121.6**	**155.3**	**173.7**	**194.2**	**204.8**	**220.0**	**241.0**	**262.7**	**281.7**	**293.1**
Income (loss) from operating	**30.6**	**(26.8)**	**(33.0)**	**(65.0)**	**(82.5)**	**(94.5)**	**46.9**	**181.4**	**314.1**	**399.8**	**484.2**	**566.5**	**651.4**	**697.7**	**682.1**
Other non-operating income (loss)															
Interest income (expense), net	(2.4)	(12)	(6.5)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Other income (expense), net	0.5	1.8	0.4	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Income (loss) from operations before tax benefit	**28.6**	**(26.2)**	**(39.1)**	**(64.5)**	**(82.0)**	**(94.0)**	**47.4**	**181.9**	**314.6**	**400.3**	**484.7**	**567.0**	**651.9**	**698.2**	**682.6**
Tax benefit	2.3	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Deemed dividend	0.0	0.0	(18.2)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Net Income (Loss)	**30.9**	**(26.2)**	**(57.3)**	**(64.5)**	**(82.0)**	**(94.0)**	**47.4**	**181.9**	**314.6**	**400.3**	**484.7**	**567.0**	**651.9**	**698.2**	**682.6**
Gain on exchange of convertible perferred stock in connection with recapitalization	0.0	160.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Less beneficial conversion charge	0.0	(0.4)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Net income attributable to common stockholders	**30.9**	**133.3**	**(57.3)**	**(64.5)**	**(82.0)**	**(94.0)**	**47.4**	**181.9**	**314.6**	**400.3**	**484.7**	**567.0**	**651.9**	**698.2**	**682.6**
Tax rate	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*3%*	*8%*	*12%*	*18%*	*27%*	*35%*	*35%*	*35%*	*35%*
Income Tax	0.0	0.0	0.0	0.0	0.0	0.0	1.4	14.5	37.7	72.0	130.9	198.4	228.2	244.4	238.9
Net income (loss) per share - basic	**23.95**	**219.76**	**(2.88)**	**(2.51)**	**(2.38)**	**(2.62)**	**1.11**	**3.97**	**6.41**	**7.29**	**7.78**	**7.96**	**8.98**	**9.45**	**8.96**
Net income (loss) per share - diluted	**4.55**	**42.50**	**(2.63)**	**(2.34)**	**(2.25)**	**(2.49)**	**1.06**	**3.80**	**6.14**	**7.00**	**7.47**	**7.65**	**8.63**	**9.09**	**8.63**
Weighted average common shares outstanding - basic	0.001	0.003	19.9	25.7	34.5	35.8	41.3	42.1	43.2	45.0	45.5	46.3	47.2	48.0	49.5
Weighted average common shares outstanding - diluted	0.006	0.017	21.8	27.6	36.4	37.7	43.2	44.0	45.1	46.9	47.4	48.2	49.1	49.9	51.4

Source: Cowen and Company

Valuation Methodology & Investment Risks

Valuation Methodology

Biotechnology:

In calculating our 12-month target price, we employ one or more valuation methodologies, which include a discounted earnings analysis, discounted cash flow analysis, net present value analysis and/or a comparable company analysis. These analyses may or may not require the use of objective measures such as price-to-earnings or price-to-sales multiples as well as subjective measures such as discount rates.

We make investment recommendations on early stage (pre-commercial) biotechnology companies based upon an assessment of their technology, the probability of pipeline success, and the potential market opportunity in the event of success. However, because these companies lack traditional financial metrics, we do not believe there are any good methodologies for assigning a specific target price to such stocks.

Investment Risks

Biotechnology:

There are multiple risks that are inherent with an investment in the biotechnology sector. Beyond systemic risk, there is also clinical, regulatory, and commercial risk. Additionally, biotechnology companies require significant amounts of capital in order to develop their clinical programs. The capital-raising environment is always changing and there is risk that necessary capital to complete development may not be readily available.

Company Specific Risks

The Phase IIb clinical trial for nmDMD and the Phase III clinical trial for nmCF that PTC completed failed to achieve the pre-specified primary endpoints with statistical significance. There is no guarantee that the ongoing and the planned Phase III clinical trials will meet the primary endpoint even though PTC has modified the trial designs to demonstrate maximum clinical benefit. Additionally, the EMA has raised questions about ataluren's insufficient efficacy and optimal dose and therefore, may reject PTC's application for conditional approval in the EU. As a result, even if the Phase III clinical trials succeed, ataluren will not be able to enter the market for several years. PTC's current balance sheet is strong but we estimate that there will be a need for additional funding to complete the trials for regulatory approval in the U.S.

Addendum

Analyst Certification

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Cowen and Company Rating System effective May 25, 2013

Outperform (1): The stock is expected to achieve a total positive return of at least 15% over the next 12 months

Market Perform (2): The stock is expected to have a total return that falls between the parameters of an Outperform and Underperform over the next 12 months

Underperform (3): Stock is expected to achieve a total negative return of at least 10% over the next 12 months

Assumption: The expected total return calculation includes anticipated dividend yield

Cowen and Company Rating System until May 25, 2013

Outperform (1): Stock expected to outperform the S&P 500

Neutral (2): Stock expected to perform in line with the S&P 500

Underperform (3): Stock expected to underperform the S&P 500

Assumptions: Time horizon is 12 months; S&P 500 is flat over forecast period

Cowen Securities, formerly known as Dahlman Rose & Company, Rating System until May 25, 2013

Buy – The fundamentals/valuations of the subject company are improving and the investment return is expected to be 5 to 15 percentage points higher than the general market return

Sell – The fundamentals/valuations of the subject company are deteriorating and the investment return is expected to be 5 to 15 percentage points lower than the general market return

Hold – The fundamentals/valuations of the subject company are neither improving nor deteriorating and the investment return is expected to be in line with the general market return

COWEN AND COMPANY RATING ALLOCATION

Distribution of Ratings/Investment Banking Services (IB) as of 06/30/13

Rating	Count	Ratings Distribution	Count	IB Services/Past 12 Months
Buy (a)	380	58.37%	48	12.63%
Hold (b)	247	37.94%	2	0.81%
Sell (c)	24	3.68%	1	4.17%

(a) Corresponds to "Outperform" rated stocks as defined in Cowen and Company, LLC's rating definitions. (b) Corresponds to "Market Perform" as defined in Cowen and Company, LLC's ratings definitions. (c) Corresponds to "Underperform" as defined in Cowen and Company, LLC's ratings definitions.

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