Celladon Corp. (CLDN)

Initiating Coverage with an OUTPERFORM and $17 PT, Put a Gene on It-Pivotal CUPID2 Heart Failure Data Due Q2:15

- **CLDN is developing MYDICAR, a gene therapy treatment for advanced heart failure, that has shown positive and disease-modifying results in a Phase I/IIa trial.** MYDICAR is a modified adeno-associated virus to deliver the SERCA2a protein to damaged heart muscle, potentially restoring contractile efficiency of the heart, the loss of which is the hallmark of heart failure.
- **The high dose (which the company is carrying forward in its Phase IIB CUPID 2 trial) of MYDICAR demonstrated a statistically significant reduction of 82% in the risk of major cardiovascular events in the Phase I/IIa CUPID 1 trial, in addition to improvements in overall survival out to 3 years.** While it was a relatively small study (39 patients total, with 9 patients in the high dose and 14 in the placebo arm), we are encouraged by the large improvements in both cardiovascular events and overall survival, and the correlation between patient improvement and higher doses.
- **MYDICAR's safety profile appears to be benign, making it straightforward to potentially integrate the therapy in the current standard of care.**
- **The European Medicines Agency (EMA) has indicated the CUPID 2 trial could provide a basis for registration, with sufficient efficacy and safety.**
- **The company has a Special Protocol Assessment (SPA) in place with the FDA, with agreement that a single, 572-patient Phase III trial, using the same endpoint as CUPID 2, could support MYDICAR's registration.**
- **With an enterprise value of ~$85M, and an extremely large market opportunity in advanced heart failure (an annual incidence of about 350,000 in the U.S. alone), and the potential for EU approval on positive CUPID 2 data, our view is that investors are currently overlooking significant opportunity in CLDN shares.**
- **Initiating coverage with an OUTPERFORM rating and $17 price target.** Our price target of $17 is derived from applying a 6 multiple to estimated 2020 sales in new heart failure patients, discounted by 35% annually, supplemented by the present value of sales in existing heart failure patients (also discounted by 35% annually).

FYE Dec	2013E	2014E			2015E		
REV	ACTUAL	CURR.	PREV.	CONS.	CURR.	PREV.	CONS.
Q1 Mar	--	0.0E		N/AE	0.0E		N/AE
Q2 Jun	0.0E	0.0E		N/AE	0.0E		N/AE
Q3 Sep	0.0E	0.0E		N/AE	0.0E		N/AE
Q4 Dec	0.0E	0.0E		N/AE	0.0E		N/AE
Year*	**0.0E**	**0.0E**		**N/AE**	**0.0E**		**N/AE**
Change	--	--			--		
	2013E	2014E			2015E		
EPS	ACTUAL	CURR.	PREV.	CONS.	CURR.	PREV.	CONS.
Q1 Mar	--	($0.42)E		--	($0.43)E		--
Q2 Jun	--	($0.39)E		--	($0.35)E		--
Q3 Sep	($0.45)E	($0.41)E		--	($0.33)E		--
Q4 Dec	($0.47)E	($0.42)E		--	($0.31)E		--
Year*	**($1.63)E**	**($1.64)E**		**--**	**($1.42)E**		**--**
P/E	--	--			--		
Change	--	-0%			13%		

Consensus estimates are from Thomson First Call.
** Numbers may not add up due to rounding.*

February 21, 2014

Price
$7.57

Rating
OUTPERFORM

12-Month Price Target
$17

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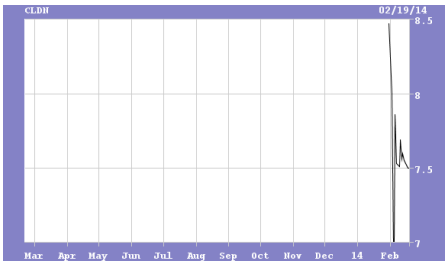
Company Information

Shares Outst (M)	18.5
Market Cap (M)	$141.0
52-Wk Range	$7.45 - $10.15
Book Value/sh	$1.24
Cash/sh	$2.93
Enterprise Value (M)	$86.8
LT Debt/Cap %	0.0
Cash Burn (M)	$18.2

Company Description

Celladon Corp. is based in San Diego, Ca. and is focused on the development of MYDICAR, a gene therapy product for increasing SERCA2a expression, currently in the Phase IIb CUPID 2 trial in advanced systolic heart failure.



Source: Thomson Reuters

Investment Thesis

Celladon Corporation (CLDN) is a biotechnology company focused on the development of MYDICAR for cardiovascular diseases characterized by deficiencies in the SERCA enzyme. Its lead clinical program is MYDICAR, a gene therapy designed to restore normal levels of the SERCA enzyme, and the company is currently enrolling patients in the Phase IIb CUPID 2 trial for the treatment of advanced systolic heart failure. MYDICAR could also be efficacious in treating other serious cardiovascular diseases, including diastolic heart failure, advanced heart failure in patients on an LVAD, pulmonary arterial hypertension, and AV-fistula maturation failure. CLDN also has small molecule SERCA modulators in preclinical development for diabetes and neurodegenerative conditions. With an enterprise value of about $85 million and the very large market opportunity in heart failure, we believe the market is undervaluing the company. We also note that with the EMA indicating that CUPID 2 could serve as the basis for an MAA application, there is a possibility that the ongoing Phase IIb study could be sufficient for early approval in the US.

Valuation

Our price target of $17 is derived from applying a 6 multiple to estimated 2020 sales in new heart failure patients, discounted by 35% annually, supplemented by the present value of sales in existing heart failure patients (also discounted by 35% annually). We estimate FDA approval for MYDICAR in 2019, and sales of $800M in 2020 from commercialization in the systolic heart failure setting. This is based on our estimates that MYDICAR could capture 35% of the patients in the US with advanced systolic heart failure who lack neutralizing antibodies to the AAV vector used in MYDICAR, with estimated pricing of $20,000 per dose. Our valuation does not take into account the additional cardiovascular applications or other preclinical programs, as we believe approval in these indications will occur after our valuation year.

Risks

Risks to the achievement of our price target include clinical failure of MYDICAR, failure to achieve regulatory approval and failure to achieve sales and earnings estimates.

Key points

- CLDN is currently trading at a ~$85M enterprise value, which in our view, offers an extremely favorable risk/reward profile given the large market opportunity for cardiovascular treatments.
- The high-dose of MYDICAR, CLDN's gene therapy for heart failure, in its Phase I/IIa CUPID 1 trial demonstrated statistically significant improvements across multiple heart failure related efficacy parameters, including an 88% reduction in the risk of major cardiovascular events.
- MYDICAR has an excellent safety profile; the SERCA2 gene is delivered to the heart via an AAV vector that has low immunogenicity and is not associated with any disease. With its safety profile, it should be straightforward to use MYDICAR in the context of the existing heart failure standard of care.
- The EMA has indicated that the Phase IIb CUPID 2 trial could serve as a basis for approval of MYDICAR, if the data supports it. We believe it is possible the FDA could follow suit, as the trial assesses the same endpoint the FDA has already approved for a pivotal study.
- With CUPID 2 potentially serving as the basis for approval in Europe and/or the USA, commercialization could occur in 2016, earlier than our current expectations, potentially providing significant upside to our current price target.
- The high expense and complications associated with standard of care for advanced heart failure, in addition to the legislative push to reduce hospital readmission rates, could result in rapid adoption of MYDICAR by cardiologists.
- CLDN has full worldwide rights to MYDICAR and is the leading gene therapy company in the cardiovascular space, which has attracted the interest of Big Pharma (Pfizer's, Novartis's and J&J's venture arms own about a quarter of the company).
- Given the efficacy and safety MYDICAR has already demonstrated, we expect the results of the CUPID 2 study to be positive. With a regulatory environment that appears supportive and a large patient population in both the U.S. and Europe we would be buyers of shares.

Celladon Corp. Overview

Celladon Corp. is based in San Diego, Ca. and is focused on the development of MYDICAR, a gene therapy product for increasing SERCA2a expression, currently in the Phase IIb CUPID 2 trial in advanced systolic heart failure.

Upcoming milestones

End of Feb:14	Complete enrollment in the Phase IIb CUPID 2 trial of MYDICAR for systolic heart failure
H1:14	Initiate Phase I/II trial of MYDICAR for advanced heart failure with LVAD
2014	Start of CELL-005 trial in patients positive for neutralizing antibodies and CELL-006 trial to assess viral shedding
April:15	Data released from Phase IIb CUPID 2 trial
2015	Meetings with FDA and EMA to discuss potential expedited approval paths
2015	Data from investigator-sponsored AGENT-HF study (France) with LVEF imaging data

Figure 1: Celladon's Product Pipeline

Product	Indication/Field	Stage of Development
MYDICAR	Systolic heart failure	Phase IIb
	Advanced heart failure with LVAD	Phase I/II (start H1:14)
	Diastolic heart failure	Phase I/II (potential start H1:14)
	Pulmonary arterial hypertension	Preclinical
	Arteriovenous-fistula maturation failure	Preclinical
SERCA small molecule	Diabetes and neurodegenerative diseases	Preclinical

Source: Company data, Wedbush Securities, Inc.

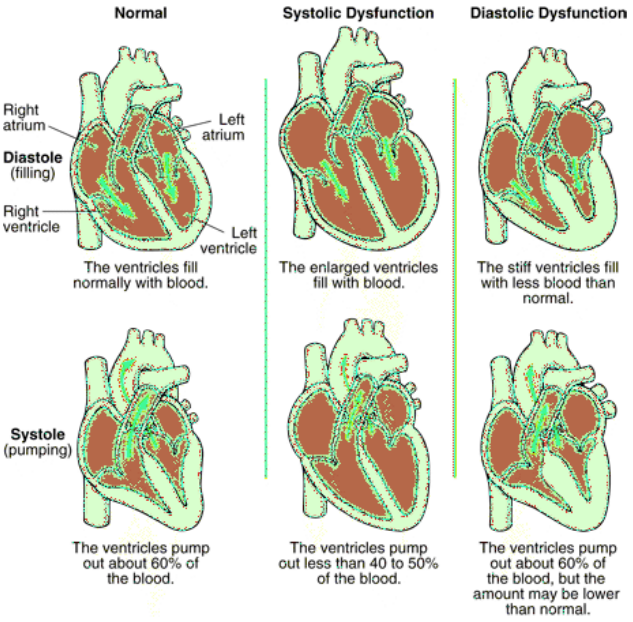
Heart Failure Background

Heart Failure

Heart failure (HF) is a chronic condition in which the heart is in a weakened state and unable to supply the body with enough blood and oxygen. The heart pumps blood to the body and the lungs through organized contractions of its four chambers (the cardiac cycle), with the atria receiving the blood and pushing it into the ventricles (diastole phase), and the ventricles pumping it out of the heart (systole phase). The cycle is split into systemic circulation, where oxygenated blood is pumped out to the body through the left ventricle and returns to the heart via the right atria, and pulmonary circulation, where deoxygenated blood is pumped to the lungs through the right ventricle and returns to the heart via the left atrium. When the heart muscle begins to weaken, it will compensate by enlarging and pumping faster, while blood vessels constrict in order to maintain blood pressure. These measures, however, offer only temporary relief to the heart's progressive deterioration, as the cardiac enlargement (hypertrophy) leads to loss of efficiency, and a negative feedback loop reinforcing the hypertrophic response. The loss of pumping efficiency is a hallmark of heart failure. Despite improvements in survival rates, currently about half of patients with HF die within five years of diagnosis.

Heart failure typically affects the left side first, which is the side responsible for pumping oxygenated blood throughout the body. The largest chamber in the heart is the left ventricle (LV), which supplies most of the heart's pumping power. Left-sided (or LV) heart failure is characterized by the loss of efficiency in its ability to pump oxygenated blood to the body, leading to loss of perfusion of oxygenated blood throughout the body, which also has deleterious effects on the rest of the organs and tissues (many HF patients also have renal failure, peripheral edema and other complications besides decreased mobility due to fatigue). LV heart failure can be either systolic or diastolic in nature, as determined by measuring the ejection fraction (percent of total blood in the LV that is pumped out with each heartbeat) during an echocardiogram. Systolic heart failure (or reduced ejection fraction) is where the LV cannot contract normally, resulting in an inability to pump with sufficient force (ejection fraction < 35% of normal). Diastolic failure (or normal ejection fraction) is where the LV cannot relax normally due to stiffened muscles, resulting in the heart not filling with sufficient blood between heartbeats. The systolic and diastolic forms are found in approximate equal proportions in HF patients.

Figure 2: Comparing Heart Failure with Normal Heart Function

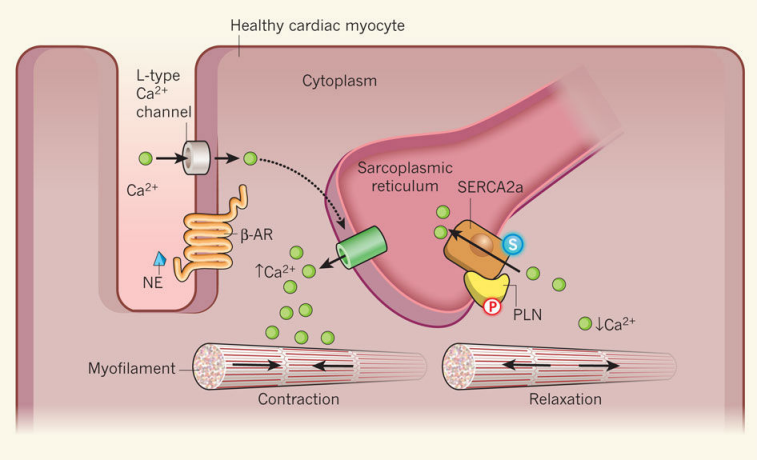


Source: The Merck Manual

SERCA2a and Its Role in Heart Muscle

One of the largest causes of altered contractile function in the LV is due to abnormal Ca^{2+} levels in cardiac muscle cells (myocytes). Calcium plays a critical role in muscle contraction. Each myofilament is surrounded by the sarcoplasmic reticulum (SR), a tubular network of membranes that regulates the calcium flow in myocytes. When the SR opens its calcium gates the cytoplasm becomes inundated with calcium, and this increased intracellular calcium concentration sets off a signaling cascade that causes the myofilaments to shorten. The release of calcium by the SR is triggered by the entry of calcium into the cell through L-type calcium channels, in a process known as calcium-induced calcium release. Once the gates close and the calcium ions return to the SR, the calcium concentration in the cytoplasm will fall and the myofilaments will relax. The calcium ions return to the SR through the sarcoplasmic reticulum Ca^{2+}-ATPase (SERCA2a), a membrane protein on the SR that acts as a calcium ion pump. SERCA2a, stimulated by SUMO1 (small ubiquitin-like modifier 1) and noradrenaline via phosphorylation of phospholamban, binds to calcium ions from the cytoplasm and hydrolyzes ATP to pump the ions back into the SR.

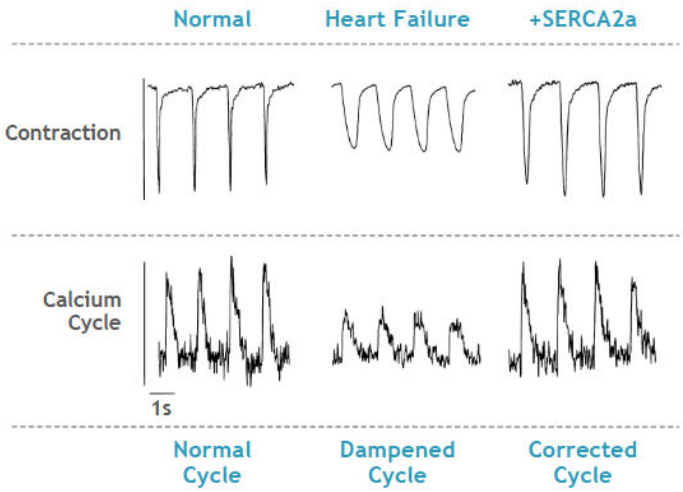
Figure 3: Calcium Regulation in Myocytes by the Sarcoplasmic Reticulum and SERCA2a



Source: Nature

A hallmark of advanced heart failure is the decreased expression and reduced activity of SERCA2a, which prevents increased cardiac output when the body is under stress. Correcting this enzyme deficiency in cells from HF patients has been found to restore the normal contractility, relaxation and calcium cycling in myocytes (see Figure 4). SERCA2a has not been fully explored as a target in heart failure due to the difficulty in increasing SERCA2a levels pharmacologically, but improvements in the safety of gene delivery have now opened up the possibility of using gene therapy to increase SERCA2a expression levels.

Figure 4: Correcting SERCA2 Deficiency in Cells from Heart Failure Patients in *In Vitro* Studies



Source: Celladon S-1

Gene Therapy

Improvements in gene therapy techniques have helped advance the technology beyond the much publicized safety concerns of the past. In 2013 Glybera (alipogene tiparvovec) became the first gene therapy to be approved in the West after the European Commission approved it to treat lipoprotein lipase (LPL) deficiency. Glybera, marketed by uniQure (QURE, Not Covered), uses an adeno-associated viral (AAV, specifically AAV1) vector to restore LPL enzyme activity. The AAV vector, which is also used in MYDICAR, offers a number of benefits over the retroviral and adenoviral vectors used for gene therapy in the past. AAVs contain no pathogens and carry no risk of insertional mutagenesis since it does not integrate into the genome, unlike the retroviruses used in the past which have carried tumorigenic risk. Retroviruses are also only able to infect dividing cells, making them an ineffective vector for heart failure since cardiac myocytes stop dividing after childhood. In comparison, AAVs are able to transfect into slow and non-dividing cells with minimal immunogenicity, allowing it to safely integrate into the target cell and stably express transgenes for an extended period. The latter characteristic also differentiates AAVs from adenoviruses, which are known for their brief expression period and for invoking strong immune reactions in patients. Adenoviruses are also known for indiscriminately infecting organs, while certain AAV serotypes have demonstrated selectivity for cardiac myocytes. Of the 12 AAV serotypes that have currently been defined, serotypes 1, 2, 6, 8 and 9 have demonstrated this selectivity and are the most widely researched vectors for gene delivery to the heart. MYDICAR (like Glybera) relies on AAV serotype 1, which in preclinical testing has been shown to be generally more effective than other AAV serotypes in transducing cardiomyocytes.

Another promising type of vector being explored for gene therapy are lentiviral vectors, which can deliver a larger genetic payload, but are considered more appropriate for systemic expression of new/altered genes (MYDICAR is delivered locally to the heart, where the expression of SERCA2a is desired). Bluebird bio (BLUE, OUTPERFORM) uses lentiviral vectors for their gene therapy platform to treat rare, systemic, genetic diseases.

Figure 5: Comparing Viral Vectors

	Retrovirus	Adenovirus	AAV	Lentivirus
Genetic material	RNA	Double-stranded DNA	Single-stranded DNA	RNA
Genome size	3-9 kb	~40 kb	5 kb	10 kb
Insertion Capacity	8 kb	30 kb	< 5kb	10 kb
Gene Expression	Stable	Brief	Stable	Stable
Infects non-dividing cells?	No	Yes	Yes	Yes
Integrates into target genome?	Yes	No	No (unless wild-type)	Yes
Risk of adverse events	Moderate	High	Lowest	Low

Source: Wedbush Securities, Inc.

Diagnostic

A major obstacle to using AAVs in gene therapy is the high prevalence of neutralizing antibodies in humans. Neutralizing antibodies (nAbs) are formed in patients as a result of previous exposure to AAVs and their presence limits the effectiveness of *in vivo* gene transfer. Even a low titer of these nAbs can prevent vector transduction, rendering any AAV-based treatment useless. This limits the potential patient population for MYDICAR, since a majority of people worldwide are exposed via natural infections to wild-type AAV by adulthood. Large international studies conducted during the 1970s found that 30-80% of humans worldwide have antibodies for AAV1 and AAV2 (Calcedoa et al. "Worldwide Epidemiology of Neutralizing Antibodies to Adeno-Associated Viruses", *Journal of Infectious Diseases* 2009). More recently, a French study found that 67% of healthy volunteers carried nAbs to AAV1 (Boutin et al. "Prevalence of Serum IgG and Neutralizing Factors Against Adeno-Associated Virus (AAV) Types 1, 2, 5, 6, 8, and 9 in the Healthy Population: Implications for Gene Therapy Using AAV Vectors", *Human Gene Therapy* 2010). However, the heart failure market opportunity is quite large, and so even a reduction in available patients of this magnitude leaves a still attractive opportunity.

CLDN has estimated that 60% of HF patients will have nAbs for the proteins in the AAV1 capsid, and has developed a companion diagnostic to exclude these patients from the MYDICAR clinical trials. The company expects to have to seek regulatory approval for any diagnostic prior to commercial use, and if approved, contract out the manufacturing to a third party. CLDN has an exclusive worldwide sublicense from AmpliPhi Biosciences Corp. (which in turn in-licensed them from the University of Pennsylvania) to patents related to AAV1 vectors for the development, manufacture, use and sale of companion diagnostics to MYDICAR. AmpliPhi receives a $310,000 annual fee and is eligible for $850,000 in milestones and a single-digit royalty on sales of the diagnostic.

Manufacturing

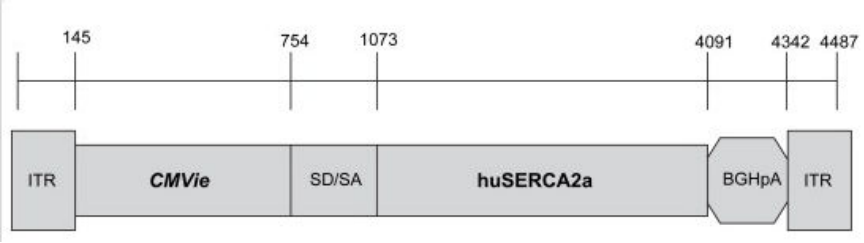
Reliably and economically manufacturing AAVs on a large scale has historically been hindered by low yields of production. CLDN has developed a scalable manufacturing process based on the same methods used for producing recombinant mAbs and proteins. The production system uses cell-suspension-based culturing techniques and stirred tank bioreactors, with the purification done with industrial chromatography. This year, CLDN plans to transfer technology and contract out the manufacturing of MYDICAR to Lonza, an experienced biopharmaceutical manufacturer that will scale up production to targeted commercial levels.

MYDICAR

MYDICAR is designed to correct the SERCA2a enzyme deficiency in HF patients by delivering the gene for SERCA2a to the heart in an AAV vector. It is created by removing the viral genes in an AAV serotype 1 capsid and replacing it with an expression cassette containing:
-the ATP2A2 gene, which encodes for SERCA2a;
-a human cytomegalovirus immediate-early enhancer (CMVie), coupled with a hybrid intron from plasmid PCI, which is a commonly used promoter used to increase and efficiently drive gene expression;
-and a bovine growth hormone polyadenylation signal (BGHpA), which is included for effective translation of the transgene mRNA.

The gene expression cassette is flanked by two small inverted terminal repeats (ITR) that are needed as signals for packaging the DNA genome into the capsid. The combined vector is comprised of a single-strand of 4486 DNA nucleotides in its entirety, with the ITRs contributing 145 bases each, the CMVie 609 bases, the PCI primer 319 bases, the SERCA2a coding sequence 3018 bases, and the BGHpA signal 251 bases.

Figure 6: Schematic of MYDICAR AAV Vector



Source: Hajjar et al. Design of a Phase 1/2 Trial of Intracoronary Administration of AAV1/SERCA2a in Patients with Heart Failure. *Journal of Cardiac Failure* (5), 14.2008

The vector is formulated in a saline buffer and can be infused directly to the heart by percutaneous catheterization through a femoral artery, a relatively simple, common procedure in the cardiologist setting. The capsid targets the vector to the cardiomyocytes, at which time the vector will insert itself into the cell and deliver the encoding DNA genome.

IP

CLDN is the sole owner of two patent families that covers the method of treating cardiovascular (CV) disease by direct infusion of a therapeutic polynucleotide into coronary circulation, including one issued patent (No. 8,221,738; expires in 2030) that also includes claims of the use of a vasodilator in combination. The company has also in-licensed two patent families related to recombinant AAV vectors, including an exclusive, worldwide license from AmpliPhi for IP covering AAV vectors and their manufacture.

Animal Testing

Preclinical testing in animal models of heart failure confirmed that overexpression of SERCA2a by AAV-mediated gene transfer preserved systolic function. The administration of MYDICAR in multiple animal models of heart failure (including rodents, sheep, canines and mini-pigs) demonstrated restored SERCA2a expression and a corresponding improvement in heart function. Long-term expression of SERCA2a was also established in a rat model of heart failure, with stable SERCA2a expression observed for up to one year post-dosing.

The pharmacological benefit of MYDICAR was established in a pig model of heart failure. In swines with heart failure induced by surgical disruption (on day 0) of the mitral valve, a single dose (1 x10 ^{12}DNase resistant particles) of MYDICAR delivered via intracoronary infusion (on day 56) significantly improved cardiac function versus placebo by day 112. Significant improvements were seen across multiple cardiac function parameters, including an absolute increase of 16% in median ejection fraction in MYDICAR treated animals versus placebo. The MYDICAR treated animals also had a significant median 14% relative decrease in end systolic volume, indicating reversal of the remodeling process (a strong predictor of lower long-term mortality and heart failure clinical events). No signs of toxicity were observed in the animals in the MYDICAR group.

Figure 7: Cardiac Function Improvement in Porcine Model of Heart Failure

	Absolute (Relative) Median Change Day 56 to Day 112*		
Cardiac Function Parameters	**Placebo**	**MYDICAR**	**p-value**
Fractional Shortening	-0.8% (-2%)	**+8% (+26%)**	**0.05**
Ejection Fraction	-5.5% (-8%)	**+10.8% (+18%)**	**0.04**
Cardiac Output	+3.4 mL/min (+60%)	**+5.9 mL/min (+94%)**	**0.05**
End Systolic Volume	+16.0 mL (+35%)	**-9.9 mL (-14%)**	**0.02**
End Diastolic Volume	+45.4 mL (+30%)	**+10.7 mL (+8%)**	**ns**
dP/dt	-41 mmHG/sec (-3%)	**+466 mmHg/sec (+33%)**	**ns**

Source: Celladon

SERCA2a expression increased alongside an improvement in biomarker levels in MYDICAR-treated animals compared to control at day 112, indicating a slower progression of HF.

The safety of MYDICAR was further established in a study in mini-pigs, with the animals being administered a dose of about $5x10^{12}$ DNase resistant particles (Drp). Despite being administered a dose that is three times larger (on a weight-adjusted basis) than the high dose given to humans in CUPID1, no toxicity or mortalities were observed in the mini-pigs at up to 90 days post-dosing.

Clinical Studies

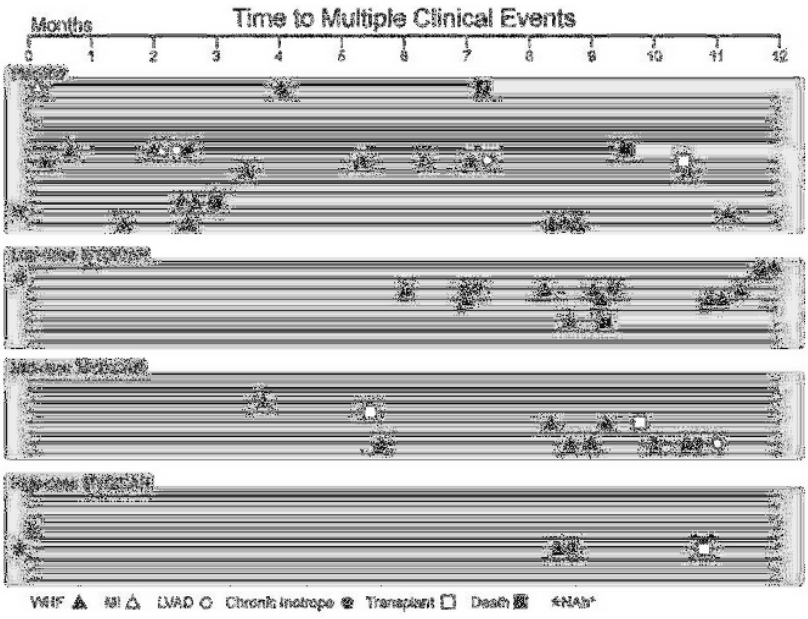
Phase I/IIa CUPID 1

The first in-human study of MYDICAR was the open-label dose-ascending Phase I portion of the CUPID1 trial, which evaluated a single intracoronary infusion of MYDCAR in 12 patients with advanced HF who received concurrent maximal optimized HF therapy. Patients were administered a 10-minute infusion of 1.4 $x10^{11}$ to 1 $x10^{13}$ Drp per patient. MYDICAR was safe and well tolerated, with no treatment-related toxicities observed in the study. Initial signs of efficacy were demonstrated across multiple HF-related parameters, including:
-LV function recovery (as determined by EF and end-systolic volume);
-symptomatic improvement (as determined by New York Heart Association and Minnesota Living with Heart Failure Questionnaire);
-functional improvement (as determined by six-minute walk test and peak maximum oxygen consumption);
-and reductions in N-terminal prohormone brain natriuretic peptide (NT-ProBNP) levels, a biomarker for CV disease.

The Phase IIa stage further expanded upon MYDICAR's performance across these four parameters. The study enrolled 39 patients with advanced HF who received one of three doses (6 $x10^{11}$, 3 $x10^{12}$, or 1 $x10^{13}$ Drp) of MYDICAR or saline placebo on top of maximal optimized HF therapy. Enrolled patients were prescreened for nAb-negative status, although three developed AAV1 nAbs between their initial selection into the study and time of dosing. The primary endpoint was improvement across multiple parameters without significant worsening in any single one.

The high dose (n=9) of MYDICAR met the primary endpoint vs. placebo (HR=0.12, p=0.003) at six months, with improvements/stabilization seen across the four efficacy parameters. The results were confirmed at 12 months, which also showed that MYDICAR delayed the time patients suffered clinical events compared to placebo, with the strongest benefit seen in the high-dose group. Clinical events were grouped as incidents of worsening heart failure (WHF), myocardial infarction (MI), LVAD implantation, use of chronic IV inotrope, heart transplant or death, with WHF defined as signs and symptoms of HF requiring either hospitalization or treatment with IV diuretics, vasodilators/positive inotropes, intra-aortic balloon pump or mechanical fluid removal. Of note, in the high-dose group, one of two patients with worsening heart failure had nAbs at the time of dosing.

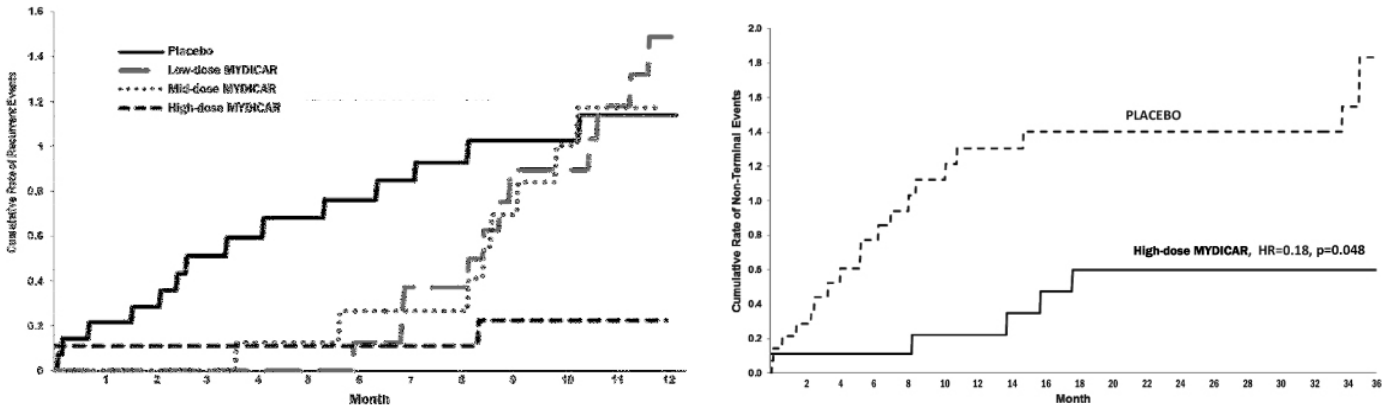
Figure 8: Time to Multiple Clinical Events in Phase IIa Trial



Source: Celladon S-1. Note: each line represents a patient

All MYDICAR doses reduced the frequency of cardiovascular events (WHF and MI), with only the high-dose group producing a durable response (see Figure 9). At three years follow-up the frequency of non-terminal events was reduced by 82% (p=0.048) with high-dose MYDICAR versus placebo. Analysis of heart tissue samples collected from patients who later died or received an LVAD or heart transplant showed that AAV1/SERCA2a vector DNA was detected in samples from only patients in the high-dose group, with the longest persistence seen in a biopsy sample collected at 31 months post-administration. The absence of MYDICAR in the samples from patients in the low- and mid-dose groups indicates that the highest dose was sufficient to insert the SERCA2a gene durably. In our opinion, it also likely explains the lower efficacy seen in the lower-dose groups.

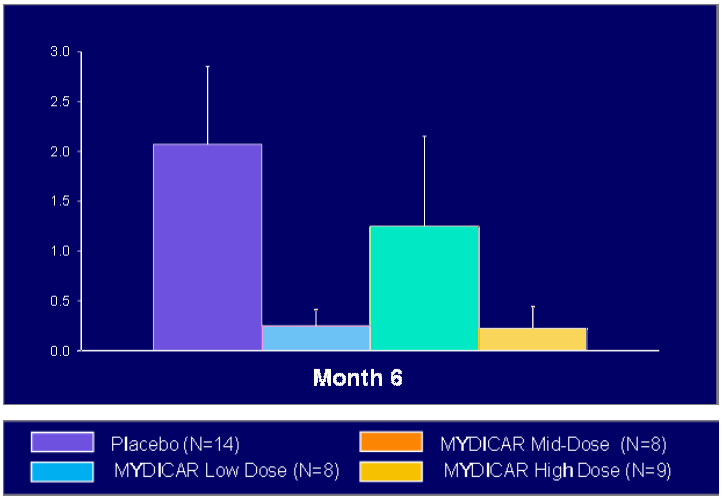
Figure 9: Frequency of Cardiovascular Events at 12 and 36 months



Source: Celladon S-1

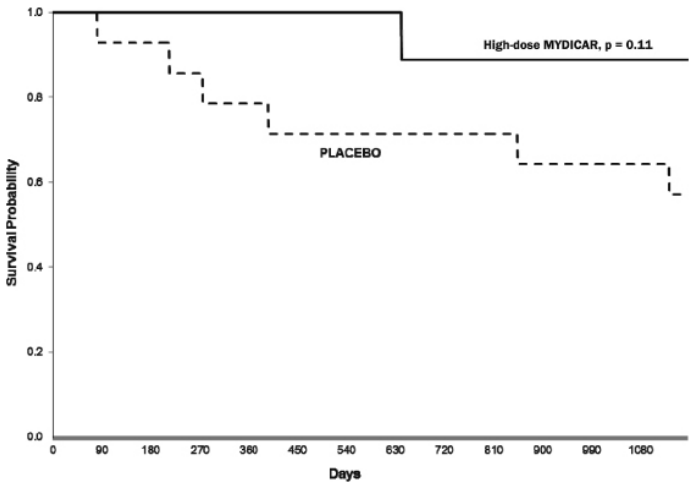
The severity of the HF-related hospitalizations was reduced with MYDICAR, with the mean duration of HF-related hospitalization during the 12 months being significantly lessened (0.4 vs. 4.5 days, p=0.05) with high-dose MYDICAR vs. placebo (Figure 10). MYDICAR also showed a trend in improved long-term survival, with 89% of high-dose group alive at three years post-administration compared to 63% in the mid- and low-dose groups and 57% in the placebo arm (Figure 11).Over the three year follow up MYDICAR demonstrated an excellent safety profile, with no increases seen in AEs, HF-related events or laboratory abnormalities versus placebo.

Figure 10: Mean Days of CV-related Hospitalization



Source: Celladon S-1

Figure 11: Survival Benefit at Three Years



Source: Celladon S-1

Figure 12: Safety Summary at 12 months

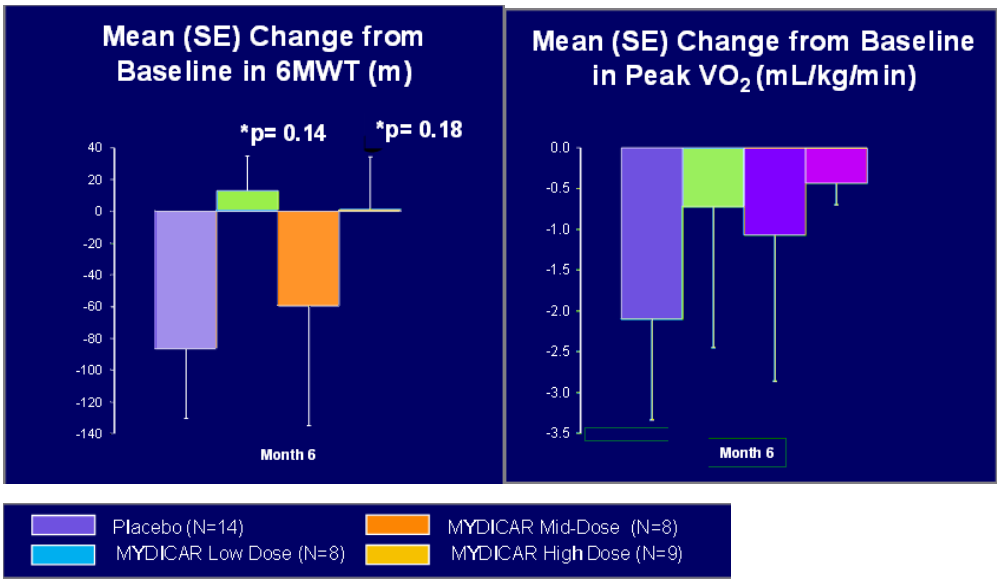
	Placebo N=14	Low-dose MYDICAR N=8	Mid-dose MYDICAR N=8	High-dose MYDICAR N=9
Any AE	13 (93%)	8 (100%)	8 (100%)	8 (89%)
Any SAE	9 (64%)	5 (63%)	4 (50%)	3 (33%)
Deaths	3 (21%)	1 (13%)	0	0
Deaths at 3 yrs	6 (43%)	3 (38%)	3 (38%)	1 (13%)

Source: Celladon, Wedbush Securities, Inc.

Improvements with MYDICAR treatment were seen across the four efficacy parameters compared to placebo. At six months, high-dose MYDICAR reduced the decline from baseline in the six-minute walk test (6MWT) and peak maximum oxygen consumption (VO_2). High-dose MYDICAR also produced large declines in New York Heart Association (NYHA) and Minnesota Living with Heart Failure Questionnaire (MLWHFQ) scores compared to placebo (note that higher scores correlate to a poorer quality of life).

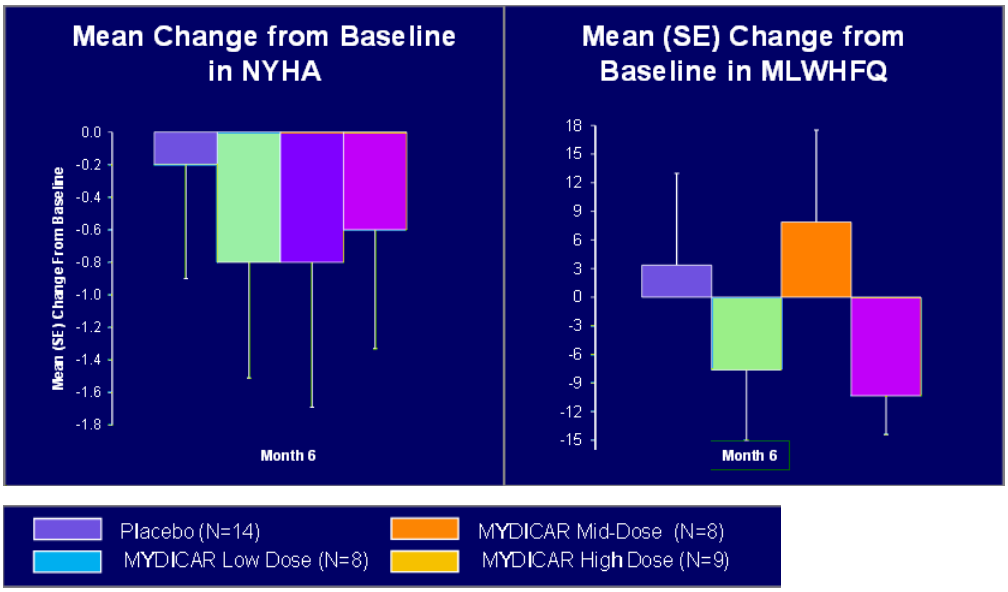
Particularly noteworthy in our view was that high-dose MYDICAR also reduced the decline in ejection fraction and reduced the end-systolic volume in the left ventricle at six months compared to placebo, showing potentially real disease-modifying activity for MYDICAR. Levels of NT-ProBNP, a peptide released by the heart typically in response to HF, were also lower in MYDICAR-treated patients compared to placebo.

Figure 13: Change in Functional Domain



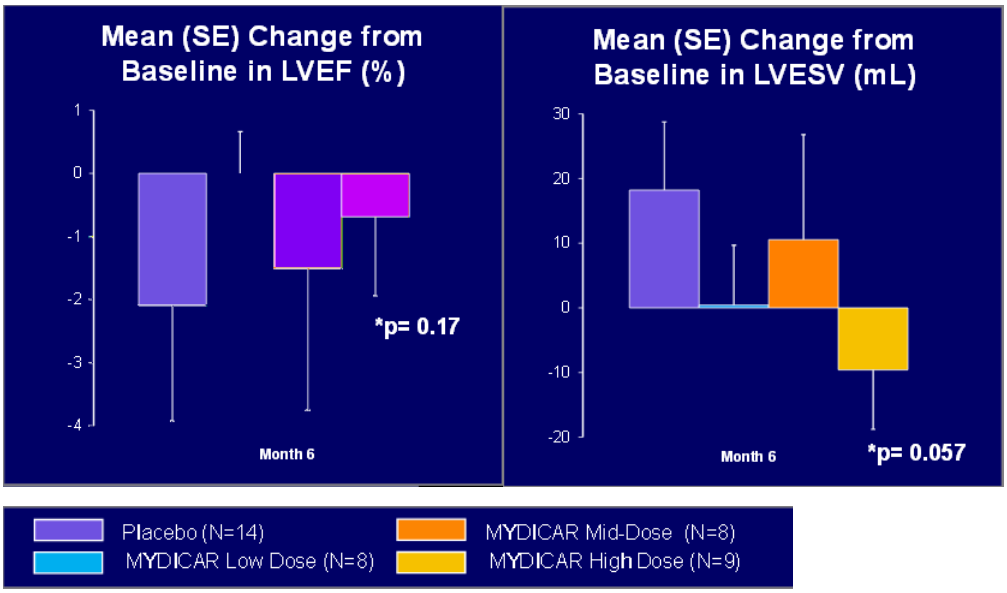
Source: Celladon

Figure 14: Change in Symptomatic Domain



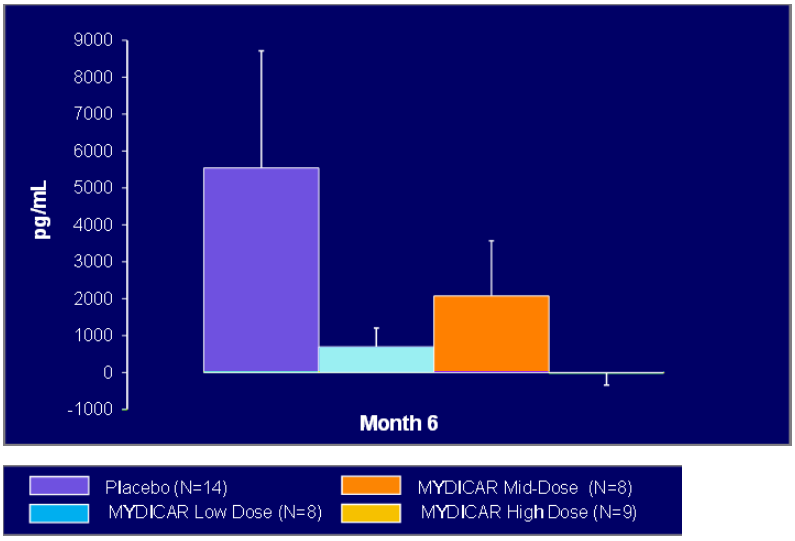
Source: Celladon

Figure 15: Change in LV Function: Ejection Fraction (left) and End Systolic Volume (right)



Source: Celladon

Figure 16: Change in Biomarker Levels



Source: Celladon

CUPID 2

The blinded Phase IIb 'CUPID 2' trial is currently enrolling ~250 patients with advanced (as determined by presence of elevated natriuretic peptides or recent HF-related hospitalization, and NYHA class II-IV heart failure) systolic HF across ~60 international sites, with enrollment expected to complete by the end of February. Patients will be screened for the presence of AAV neutralizing antibodies, and then randomized 1:1 to high-dose MYDICAR or placebo while continuing to receive maximal optimized HF therapy. Patients will receive a single intracoronary infusion and be observed for 12 months with an additional 12-month follow up. The primary endpoint is time-to-recurrent HF related hospitalizations in the presence of terminal events, calculated using a joint frailty model. Additional endpoints include time-to-first terminal event, 6MWT and QoL questionnaire. The trial, which is 83% powered ($p<0.05$) to detect a 45% risk reduction of cardiovascular events, will be unblinded after all patients have completed the 12-month observation period and at least 186 HF-related hospitalizations have occurred. Results from CUPID 2 are expected in April 2015.

Outlook

Since CUPID 2 uses the same endpoint the FDA supported for a pivotal Phase III study, it is possible that sufficiently positive results in CUPID 2 could serve as the basis for a BLA filing. CUPID 2 serving as a registration study would parallel the decision made by EMA's Committee for Medicinal Products for Human Use (CHMP), which in late 2013 indicated that a significant clinical benefit and clean safety profile for MYDICAR in CUPID 2 would be sufficient to support an MAA. If the FDA does require a Phase III trial, CLDN does have its SPA in place for a 572-patient trial using the same endpoint.

The FDA granted CLDN an SPA for a single 572-patient Phase III trial using high-dose MYDICAR with a primary efficacy endpoint of time-to-recurrent HF related hospitalizations in the presence of terminal events (all-cause death/heart transplant/LVAD implantation), and indicated support for CLDN's proposed safety database size of 610 patients (one-half treated).

The agreement by the FDA to the composite primary endpoint should allow for the disease burden of HF to be captured more fully and provide a more complete picture of MYDICAR's treatment benefit. Using the endpoint reduces the likelihood of a study being underpowered at a given patient size, and also takes into account quality-of-life factors as recurrent hospitalizations are a strong sign of distress in patients. Discussions with the FDA are still ongoing regarding the use of joint frailty model (which estimates the distinct effect treatment has on disease recurrence and survival, while taking into account the association between the two parameters) as the statistical method to analyze the composite endpoint.

Other Clinical Studies

The AGENT-HF trial is an ongoing investigator-initiated French study to determine if MYDICAR can reverse the HF-related decline in the function and physiology of the LV. The study will randomize about 44 HF patients 1:1 to receive MYDICAR or placebo, with the primary endpoint being change from baseline in LV end systolic volume (as measured by cardiac CT) at six months.

The Phase I/II CELL-005 trial will evaluate the safety of MYDICAR in patients who are positive for AAV1 nAbs. The FDA is mandating this safety trial to cover the possibility that (if approved) MYDICAR may be used off-label in the nAb positive patient population. The efficacy of MDYICAR will also be assessed, although the study is not powered to show significance. The trial is expected to start this year and enroll about 70 patients.

The CELL-006 trial is a viral shedding study that will seek to determine how long patients are excreting MYDICAR and potentially putting others at risk. Patients will be followed until they have two consecutive bodily fluid samples that are negative for presence of the SERCA2a gene, with an additional two year safety follow-up. The trial is set to start this year and will enroll 10-20 HF patients who will be treated with high-dose MYDICAR.

Current Treatments

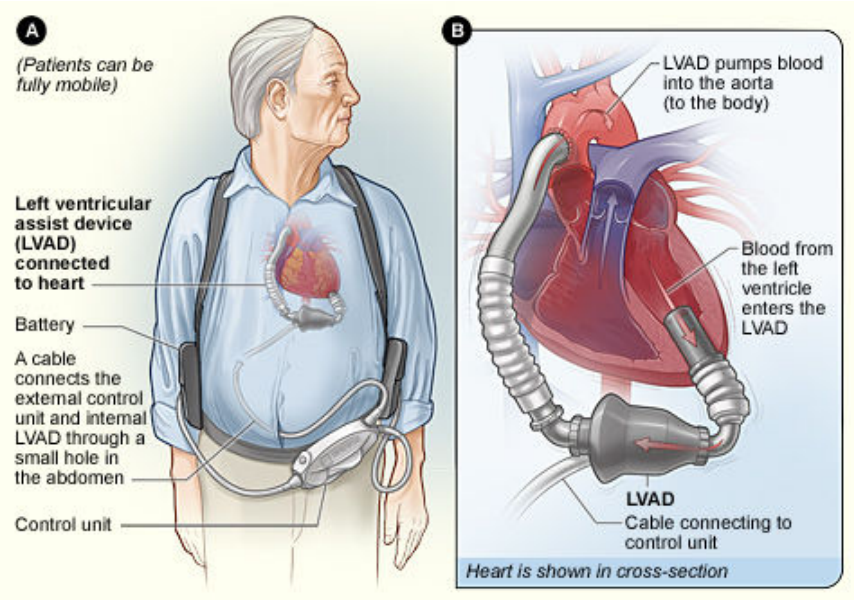
Current treatments for heart failure vary based on its severity and underlying cause. The severity of HF can be determined by the impact its symptoms have on patients. Advanced HF, staged as Class III and IV on the NYHA classification system, is where patients have significant limitations on physical activity and suffer from fatigue and pain even when at rest. The underlying cause of HF can be diseases like atherosclerosis and hypertension or a contributing condition like a prior heart attack.

After lifestyle changes, the first line treatment for patients with reduced LV systolic function are angiotensin-converting enzyme (ACE) inhibitors. In patients who do remain symptomatic or are intolerant of ACE inhibitor therapy, angiotensin II type I receptor blockers (ARB) can be used as an alternative blood vessel dilator. Since the majority of severe HF patients also show signs of fluid retention, diuretics are typically administered. A standard treatment regimen will also include aldosterone receptor antagonists and beta-adrenergic receptor blockers, commonly referred to as beta-blockers. Beta-blockers inhibit normal epinephrine and norepinephrine-mediated sympathetic actions, resulting in a reduction in the physical exertion on heart rate and force of contraction. Patients who fail to stabilize following treatment with beta-blockers and vasodilators and have recurring hospitalizations typically receive digoxin. For severe HF that leads to hypoperfusion (decreased blood flow characterized by a systolic blood pressure < 80 mm Hg) the recommended treatment is an IV inotropic agent to improve contractility.

For end-stage HF, the only curative treatment option is heart transplantation. Heart transplant outcomes have improved due to advances in immunosuppressive therapy, with 88% of recipients (who before transplant had typically less than a year to live) surviving the first year after transplant. The five and ten-year survival rate is 75% and 56%, respectively, with the average post-operation survival being about 15 years. Despite the proven therapeutic benefit, the use of heart transplantation has been limited due to the small number of available hearts. Only about 3,500 heart transplants are performed each year, with the majority (about 2,500) performed in the US.

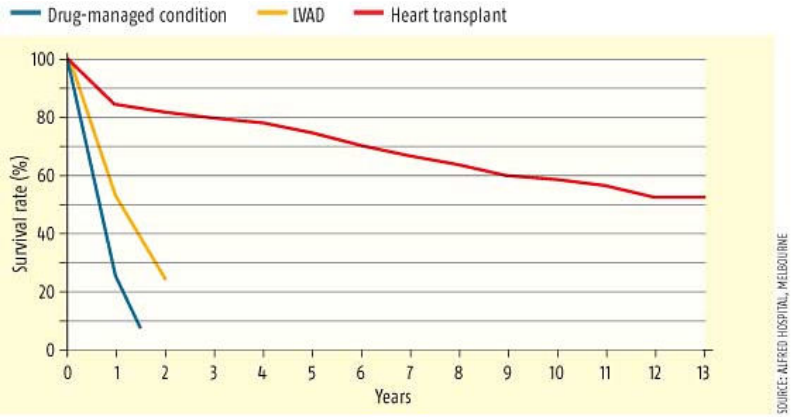
For patients who are waiting for a donor heart to become available, a left ventricular assist device (LVAD) can be implanted under the skin in the upper abdomen to help pump blood through the body. Originally designed to be a temporary implant, advancements in the device's longevity and size (akin to a cigarette pack today) have made LVADs a permanent solution for advanced heart failure patients. Although they can act as a long-term mechanical heart, the survival rate for LVADs are lower compared to heart transplantation (see Figure 18). LVADs also introduce inconveniences like daily charging requirements for the device's internal battery via a wire that extends from the patient's abdomen. About 5,500 LVADs were implanted worldwide in 2012, including about 1,000 in the US.

Figure 17: Implantable LVADs



Source: NIH: National Heart, Lung and Blood Institute

Figure 18: Survival in Advanced Heart Failure



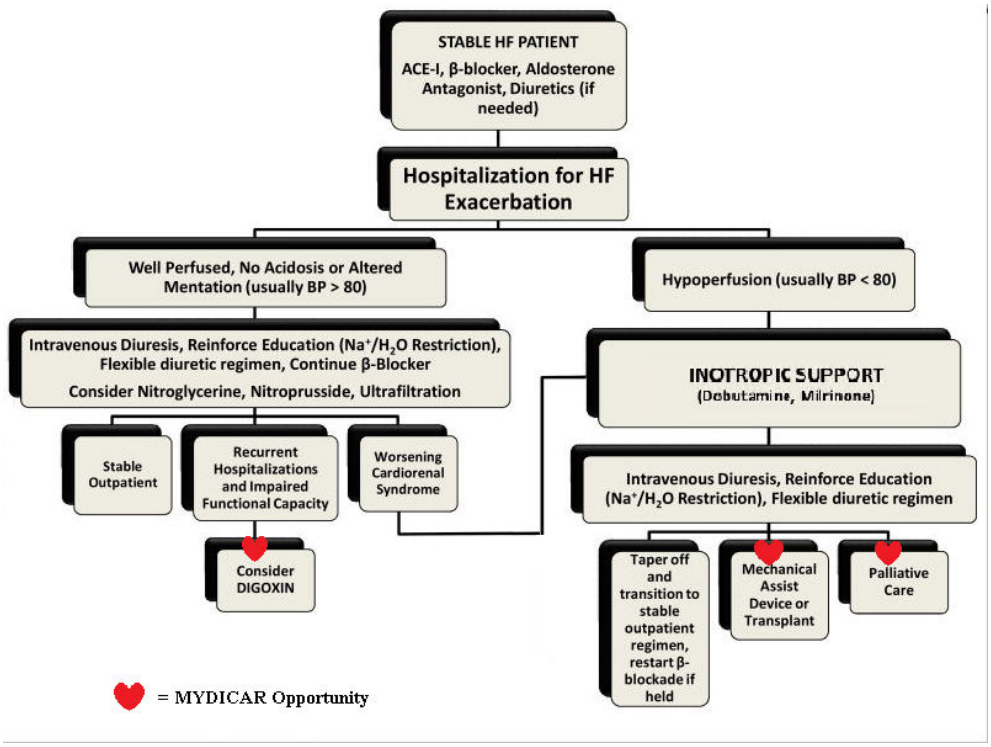
Source: Alfred Hospital, Melbourne (New Scientist)

Market

The initial target market for MYDICAR is in end-stage patients being considered for a heart transplant or LVAD implantation. The scarcity of available hearts and the risks associated with these surgical procedures provides a strong clinical value proposition for MYDICAR. We believe the market for MYDICAR can be expanded to include patients with recurring hospitalization and impaired

functional capacity. The recommended treatment for these patients is oral digoxin, which produces a mild inotropic effect without the substantial toxicity associated with intravenous inotropes (the two most commonly used IV inotropes, dobutamine and milrinone, produces symptomatic improvement, but increases mortality with long-term use). Considering that digoxin has been found to only slightly reduce symptoms with no improvement in survival, MYDICAR's clean safety profile and demonstrated survival benefit should make it a compelling alternative.

Figure 19: Role of MYDICAR Within Current Treatment Practice for Heart Failure

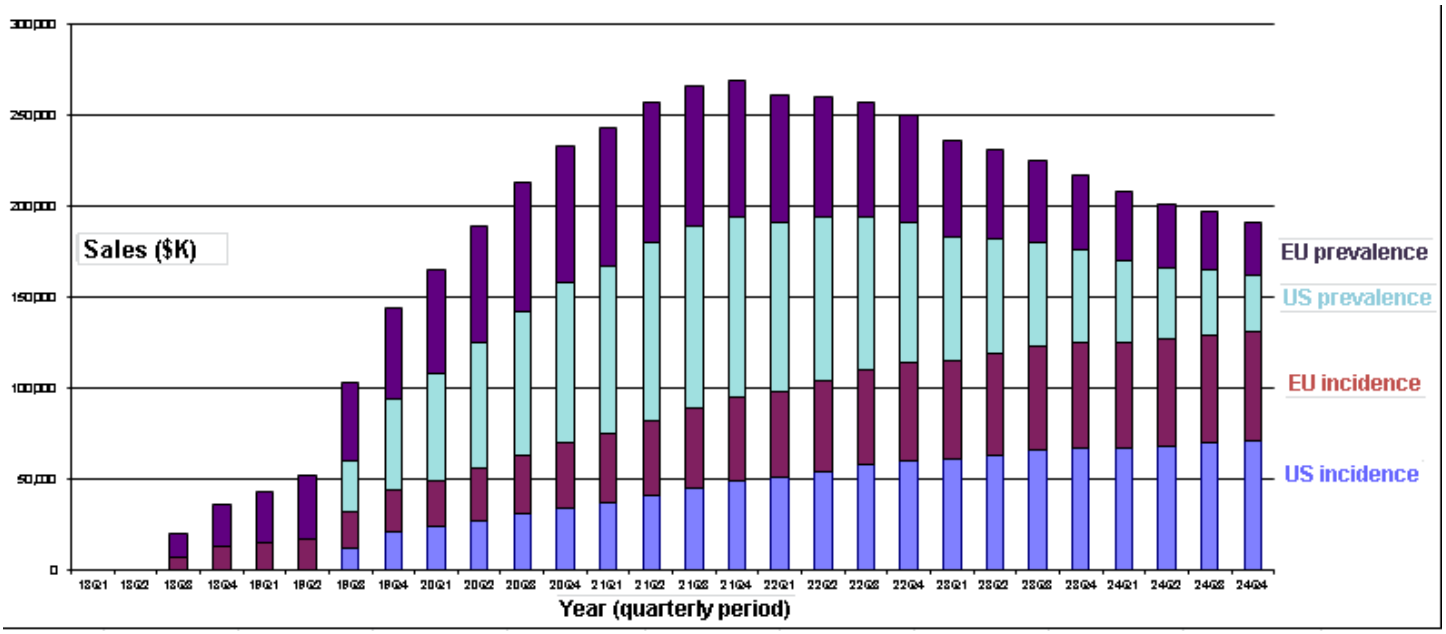


Source: Adapted from Goldhaber, J. "Role of Inotropic Agents in the Treatment of Heart Failure" Circulation (2010), 121

We estimate that there are currently 900,000 HF patients in the US who are functionally impaired and have reached end-stage status, with an additional ~120,000 patients deteriorating to that level each year. Of these patients, approximately 60% may have nAbs that make them ineligible for MYDICAR treatment. In this segment MYDICAR should be able to command premium pricing due to the economic burden associated with HF; the estimated cost of a heart transplant or LVAD implantation is nearly $170,000 in the US. To be conservative, we assign a price for MYDICAR based on a cost/benefit analysis of hospitalization costs. The cost of hospitalizing a HF patient averages $5,000 per day, and recall that in CUPID 1 MYDICAR produced a ~4-day reduction in the average duration of HF-related hospitalization in the 12 months after dosing versus untreated patients (0.4 vs. 4.5 days, $p<0.05$). Based on this we believe MYDICAR could sell for at least $20,000 per dose, providing a >90% gross margin on the estimated cost of goods of $1,500 per dose.

We expect approval in Europe in 2018 and the US in 2019 to lead to $801M in sales in 2020, our valuation year (note that we do not expect MYDICAR to be approved in territories outside of Europe and the US prior to 2020). Looking out through 2024, we expect sales in Europe and the US to peak in late 2021 and then gradually decline and stabilize as the majority of the prevalent HF population are treated. This declining prevalence model, similar to that seen in the hepatitis C market, is characterized by a large but limited-duration opportunity and underscores the importance of first-mover advantage. However, unlike the hepatitis C market, there is a large, continuing incident patient population that should continue to provide an attractive opportunity for MYDICAR.

Figure 20: Sales Forecast Through 2024



Source: Wedbush Securities

CLDN is likely to build its own sales force to market in the US, while seeking a partner in international territories. In the US CLDN will likely target cardiologists in hospitals and large medical centers that are expected to be the first adopters of MYDICAR. In the US there are currently about 125 hospitals that offer heart transplants and about 15,000 practicing cardiologists, and we believe CLDN should be able to target the high-prescribing cardiologists in the country with a sales force of about 100. Since MYDICAR can be delivered directly to the heart through an antegrade epicardial coronary artery infusion (AECAI), a routine procedure involving a 10-minute infusion into the groin or arm, the target market can eventually be expanded to cardiologists practicing in small clinics and other outpatient settings. Percutaneous femoral access for cardiac catherization is also a commonly used procedure that cardiologists are already familiar with, necessitating little training on the part of CLDN on how to administer MYDICAR. We also believe hospital administrators who are seeking ways to reduce readmission rates would be particularly supportive of MYDICAR, given that the approved endpoint is time to recurrent HF-related hospitalizations. Note that under the Affordable Care Ac,t hospitals suffer penalties to Medicare reimbursement if a patient readmits to the ER within 30 days of discharge. Currently about 25% of HF patients readmit to hospitals within a month after discharge, with the figure rising to 50% by six months.

Competition

There are other firms working on gene therapies for heart failure, although they are all behind in development. The furthest advanced of these competitors are Renova Therapeutics and Juventas Therapeutics. Renova is currently recruiting patients with congestive heart failure in a Phase I/II trial for their AAV serotype 5 vector carrying the gene for human adenylyl cyclase type 6, while Juventas is enrolling heart failure patients for a Phase II study of its non-viral plasmid carrying the gene for stromal cell-derived factor-1.

However, assuming MYDICAR gets past the regulatory hurdles that exist for gene therapies in the West, we view the primary competition for MYDICAR to be overcoming the traditional treatment paradigm for HF. The cardiovascular disease market is dominated by large pharmaceutical and medical device firms marketing traditional pharmacological and surgical treatments, and convincing physicians to adopt gene therapy as an alternative is, in our opinion, the major challenge CLDN faces, and one that positive data will likely surmount.

Additional Indications

Modulating SERCA2a expression has other cardiovascular applications outside of treating systolic HF, including the treatment of advanced HF in patients on an LVAD and diastolic heart failure. Additional CV applications are in treating pulmonary arterial hypertension (PAH) and arteriovenous (AV) fistula maturation failure, characterized by SERCA2a deficiency in vascular smooth muscle cells. The clinical development of MYDICAR in these additional indications are likely to be done on an opportunistic basis, and as a

result, we do not include in our model any sales in these disorders as we believe approval will not occur prior to 2020, our valuation year. Any off-label use in these indications would represent upside to our target.

Advanced Heart Failure with LVAD

Given the inconvenience and short duration of LVADs, and the increased risk of infections they carry, there is value in finding a therapeutic agent that can transition patients off of LVAD dependence. A UK study expected to start in H1:14 will explore the safety and efficacy of MYDICAR in 24 advanced HF patients on an LVAD. The patients in the study will be randomized 2:1 to MYDICAR or placebo, with heart tissue collected at six months post-treatment to determine the level of SERCA2a expression.

Diastolic Heart Failure

As with systolic failure, diastolic failure is also characterized by decreased SERCA2a expression. CLDN has conducted preclinical studies that showed the correlation of SERCA2a levels to diastolic function, and that MYDICAR administration restored SERCA2a levels and diastolic function in animal models of diastolic dysfunction. CLDN plans to initiate a pilot placebo-controlled Phase I/II study, if funding is available, evaluating the safety and preliminary efficacy of a single intracoronary infusion of high-dose MYDICAR in 40 diastolic HF patients.

Pulmonary Arterial Hypertension

PAH is an increase in the blood pressure of the arteries of the lungs, which leads to weakening of the right ventricle. Animal models of PAH that were administered MYDICAR demonstrated decreased pulmonary artery pressure and vascular remodeling compared to control. Further formulation and toxicology studies would have to be conducted to support an IND filing in this setting. CLDN co-owns with Mount Sinai a family of patents related to the use of genes, including SERCA, for the treatment of PAH.

AV-Fistula Maturation Failure

AV-fistula maturation failure is when a new AV-fistula, which is a surgically created passageway between an artery and vein designed to support dialysis in renal failure patients, becomes blocked and unusable. This occurs in about 40% of the ~100,000 fistulae placed ever year in the US. Preclinical studies have shown that increased SERCA2a expression would aid in the maintenance of the AV-fistula. Additional studies are to be completed prior to a possible IND submission.

Small Molecule Program

CLDN has a platform of small-molecule SERCA2b modulators in preclinical stage, which the company is developing for the treatment of diabetes and neurodegenerative disorders. SERCA2b, a non-muscle isoform of SERCA2a, has been found to maintain a high calcium ion concentration in the endoplasmic reticulum (ER), and this high calcium concentration is necessary for the preservation of proper ER function. Obesity has been found to disrupt intracellular calcium ion homeostasis and induce ER stress, which plays a role in the pathogenesis of diabetes. CLDN has an exclusive license to the University of Minnesota's joint ownership in a family of patents covering the high-throughput screening of small-molecule modulators of SERCA activity. CLDN currently pays an annual license fee of $120,000 to the University of Minnesota as part of the license.

Management

Figure 21: Celladon Management

Title	Biography
President and CEO: Krisztina M. Zsebo, PhD	Dr. Krisztina Zsebo has served as President and CEO since 2004. From 2004 until 2007 Dr. Zsebo was a venture partner at Enterprise Partners Venture Capital. Prior to joining Enterprise Partners, Dr. Zsebo held executive positions at Remedyne, Connetics, ALZA, Cell Genesys, and Amgen. Dr. Zsebo has a B.S. in Biochemistry from the University of Maryland, an M.S. in Biochemistry and Biophysics from Oregon State University and a Ph.D. in Comparative Biochemistry from the University of California, Berkeley.
VP of Finance and Administration: Rebecque J. Laba	Rebecque Laba has served as VP of Finance and Administration since 2007, and prior served as a consultant to Celladon on finance and administrative matters since 2005. From 1999 to 2005, Ms. Laba served in various financial and operational roles at Idun Pharmaceuticals (acquired by Pfizer in 2005). From 1997 to 1999, Ms. Laba worked at Asset Management Group, where she served in various financial and operational roles.
VP of Clinical Operations: Jeffrey J. Rudy	Jeffrey Rudy has served as VP of Clinical Operations since 2006. From 1997 to 2006, Mr. Rudy worked at Agouron Pharmaceuticals where he served in roles of increasing responsibility within its clinical research operations, including portfolio manager of the ophthalmology franchise and director of development operations. From 1995 to 1997, Mr. Rudy was at Gilead Sciences where he was clinical program manager in the clinical research department. From 1991 to 1994, Mr. Rudy worked in clinical affairs at Amgen. Mr. Rudy has a B.S. in Microbiology from Ohio State University.
VP of Manufacturing: Ryan K. Takeya	Mr. Takeya has served as VP of Manufacturing since April 2012. From 1996 to 2009, Mr. Takeya served in the Manufacturing Group at Targeted Genetics, where he oversaw in-house and contract manufacturing of clinical gene therapy products, including clinical supplies used in the MYDICAR clinical program. From 1993 to 1996, Mr. Takeya held various process development and process transfer roles at Immunex. In 2011, Mr. Takeya was at Dendreon, where he was involved with the transfer of the PROVENGE antigen manufacturing process to a secondary commercial manufacturing site. Mr. Takeya received his B.A. in Chemistry from the University of Washington.
VP of Corporate Development and Investor Relations: Fredrik Wiklund	Mr. Wiklund has served as VP of Corporate Development and Investor Relations since 2013 and before that, as Head of Corporate Development. From 2009 to 2012, Mr. Wiklund served as a consultant to Celladon on business development matters. From 2003 to 2008, Mr. Wiklund was head of corporate development and investor relations at Tercica (acquired by the Ipsen Group in 2008). From 2001 to 2003, Mr. Wiklund was at Lehman Brothers where he served in the Investment Banking Health Care Group. From 1996 to 2000, Mr. Wiklund served as an antiviral specialist at Gilead Sciences. Mr. Wiklund has a M.B.A. from the University of Southern California and a B.A. in International Relations from the University of San Diego.

Source: Celladon, Wedbush Securities, Inc.

Financial Model

CLDN raised about $38M (after expenses) in its Jan. 30 IPO, which added to its existing cash balance, should provide the company runway into the mid-2015 timeframe, after the CUPID 2 data readout is likely to occur. Assuming underwriter's option is exercised, the net proceeds from the IPO will be $44.1M. There are currently 17.7M (or 18.5M assuming underwriter's option is exercised) CLDN shares outstanding. The lock-up expiration for CLDN is July 29, 2014, at which point 12.0M shares will be eligible for sale.

Figure 22: Projected Income Statement to 2020

2/20/2014
Ticker: (CLDN:Nasdaq)
Celladon Corporation

Wedbush PacGrow Life Sciences
David M. Nierengarten, Ph.D.
415-274-6862

	2012	1H:13	Q3	Q4	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E
Revenues:												
US Product Sales	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$111,108	$411,839
ex-US Product Sales	$0	0	0	0	0	0	0	0	0	56,463	231,272	388,676
Grant Revenue	$0	0	0	0	0	0	0	0	0	0	0	0
Total Revenues	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**56,463**	**342,380**	**800,515**
Cost and Expenses:												
Cost of Sales	0	0	0	0	0	0	0	0	0	0	11,111	41,184
R&D	13,314	7,136	4,571	4,800	16,507	26,596	29,714	34,624	39,095	42,317	45,806	49,581
SG&A	2,631	1,328	952	971	3,251	4,082	4,386	4,575	4,880	12,161	35,666	110,989
Total Operating Expenses	**15,945**	**8,464**	**5,523**	**5,771**	**19,758**	**30,678**	**34,100**	**39,198**	**43,975**	**54,479**	**92,582**	**201,754**
Operating Income (Loss)	(15,945)	(8,464)	(5,523)	(5,771)	(19,758)	(30,678)	(34,100)	(39,198)	(43,975)	1,984	249,798	598,760
Net Interest Income (Expense)	(73)	44	14	57	115	1,304	1,978	3,267	3,721	2,792	5,138	15,503
Other non-operating Income (Expense)	147	(39)	56	0	0	0	0	0	0	0	0	0
Income Before Income Taxes	(15,871)	(8,459)	(5,453)	(5,713)	(19,642)	(29,375)	(32,121)	(35,931)	(40,253)	4,776	254,936	614,263
Provision for Income Taxes	0	0	0	0	0	0	0	0	0	279	7,813	192,387
Net Income (Loss)	(15,871)	(8,459)	(5,453)	(5,713)	(19,642)	(29,375)	(32,121)	(35,931)	(40,253)	4,498	247,123	421,877
GAAP EPS	**(1.58)**	-	**(0.45)**	**(0.47)**	**(1.63)**	**(1.64)**	**(1.42)**	**(1.23)**	**(1.25)**	**0.14**	**7.51**	**12.82**
Total Shares Outstanding	10,262	-	12,035	12,035	12,035	18,575	26,150	30,225	32,825	32,900	32,900	32,900
Cash Burn	-	-	-	-	(18,170)	(30,291)	(33,818)	(38,779)	(43,582)	2,847	234,539	557,955
Cash Balance	32,649	27,977	23,213	17,500	17,500	32,029	80,088	108,496	103,720	96,081	327,591	707,721

Source: Wedbush Securities

Covered Companies Mentioned

COMPANY	TICKER	RATING	PRICE	PRICE TARGET
bluebirdbio	BLUE	OUTPERFORM	$23.38	$40

Analyst Biography

David Nierengarten, Ph.D.

David is an Analyst covering stocks in the Biotechnology/Biopharmaceuticals/BioDefense sector. His prior sell-side research experience at Robert W. Baird & Co. covered biotechnology companies of all market capitalizations, with a focus on oncology and rare diseases.

David received his B.S. (Biochemistry) from the University of Wisconsin-Madison and Ph.D. (Molecular and Cell Biology) from the University of California-Berkeley.

David's Edge: David's early stage venture capital investing experience gives him a balanced perspective on developmental-stage biotechnology companies and their ultimate risk/reward potential. His experience on the other side of that equation in a clinical-stage, venture backed biotechnology company provides him with insights into corporate operations. The combination of experiences creates a focus on value creation in this event-driven space.

Analyst Certification
I, David M. Nierengarten, Ph.D., Gregory R. Wade, Ph.D., Christopher N. Marai, Ph.D., certify that the views expressed in this report accurately reflect my personal opinion and that I have not and will not, directly or indirectly, receive compensation or other payments in connection with my specific recommendations or views contained in this report.

Disclosure information regarding historical ratings and price targets is available at http://www.wedbush.com/ResearchDisclosure/DisclosureQ413.pdf

Investment Rating System:
Outperform: Expect the total return of the stock to outperform relative to the median total return of the analyst's (or the analyst's team) coverage universe over the next 6-12 months.
Neutral: Expect the total return of the stock to perform in-line with the median total return of the analyst's (or the analyst's team) coverage universe over the next 6-12 months.
Underperform: Expect the total return of the stock to underperform relative to the median total return of the analyst's (or the analyst's team) coverage universe over the next 6-12 months.

The Investment Ratings are based on the expected performance of a stock (based on anticipated total return to price target) relative to the other stocks in the analyst's coverage universe (or the analyst's team coverage).*

Rating Distribution (as of December 31, 2013)	**Investment Banking Relationships (as of December 31, 2013)**
Outperform:54% Neutral: 43% Underperform: 3%	Outperform:18% Neutral: 2% Underperform: 0%

The Distribution of Ratings is required by FINRA rules; however, WS' stock ratings of Outperform, Neutral, and Underperform most closely conform to Buy, Hold, and Sell, respectively. Please note, however, the definitions are not the same as WS' stock ratings are on a relative basis.

The analysts responsible for preparing research reports do not receive compensation based on specific investment banking activity. The analysts receive compensation that is based upon various factors including WS' total revenues, a portion of which are generated by WS' investment banking activities.

Wedbush Equity Research Disclosures as of February 21, 2014

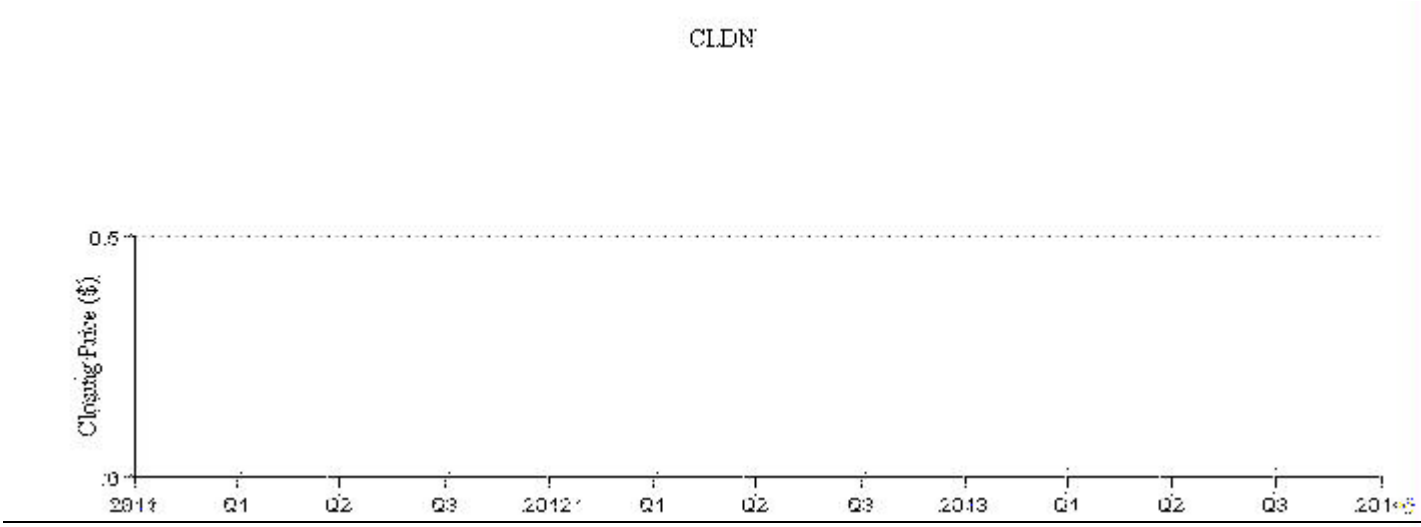
Company	Disclosure
Celladon Corp. bluebird bio	1,3,5,7 1,3,4,5

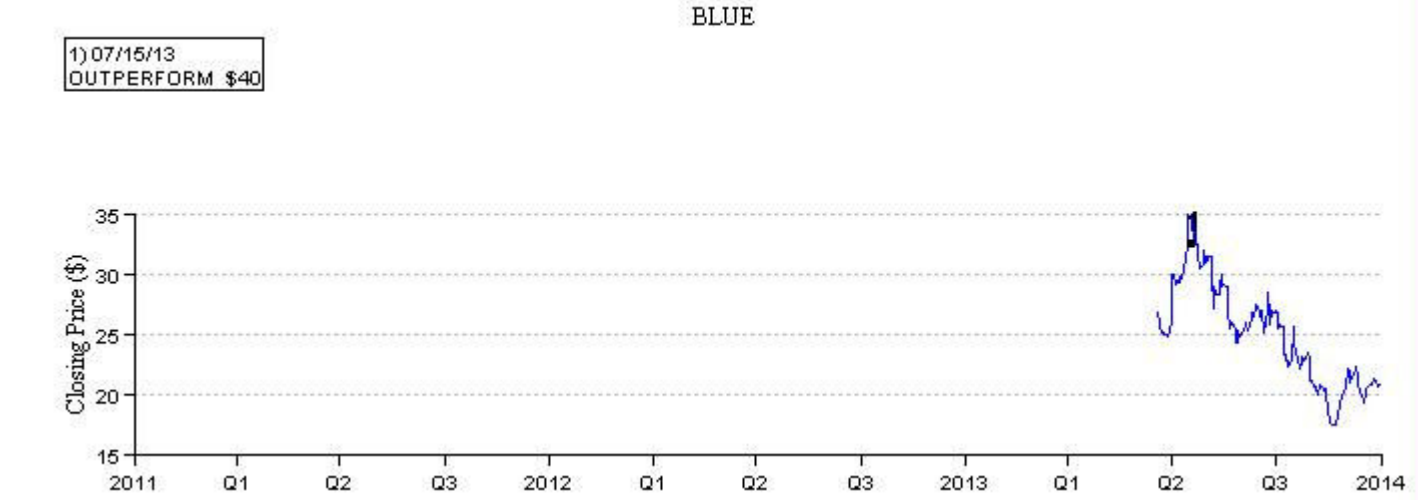
Research Disclosure Legend
1. WS makes a market in the securities of the subject company.
2. WS managed a public offering of securities within the last 12 months.
3. WS co-managed a public offering of securities within the last 12 months.
4. WS has received compensation for investment banking services within the last 12 months.
5. WS provided investment banking services within the last 12 months.

6. WS is acting as financial advisor.
7. WS expects to receive compensation for investment banking services within the next 3 months.
8. WS provided non-investment banking securities-related services within the past 12 months.
9. WS has received compensation for products and services other than investment banking services within the past 12 months.
10. The research analyst, a member of the research analyst's household, any associate of the research analyst, or any individual directly involved in the preparation of this report has a long position in the common stocks.
11. WS or one of its affiliates beneficially own 1% or more of the common equity securities.
12. The analyst maintains Contingent Value Rights that enables him/her to receive payments of cash upon the company's meeting certain clinical and regulatory milestones.

Price Charts

Wedbush disclosure price charts are updated within the first fifteen days of each new calendar quarter per FINRA regulations. Price charts for companies initiated upon in the current quarter, and rating and target price changes occurring in the current quarter, will not be displayed until the following quarter. Additional information on recommended securities is available on request.





* WS changed its rating system from (Strong Buy/Buy/Hold/Sell) to (Outperform/ Neutral/Underperform) on July 14, 2009.
Please access the attached hyperlink for WS' Coverage Universe: http://www.wedbush.com/services/cmg/equities-division/research/equity-research Applicable disclosure information is also available upon request by contacting Ellen Kang in the Research Department at (213) 688-4529, by email to ellen.kang@wedbush.com, or the Business Conduct Department at (213) 688-8090. You may also submit a written request to the following: Business Conduct Department, 1000 Wilshire Blvd., Los Angeles, CA 90017.

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