Relypsa (RLYP)

Initiating Coverage with an OUTPERFORM Rating and $34 Fair Value Based on Potential Breakthrough Treatment for Hyperkalemia

- **Relypsa is an emerging pharmaceutical company developing non-absorbed polymer drug candidates to treat renal, cardiovascular and metabolic diseases.** Patiromer is the lead drug candidate and is a non-absorbed, optimized potassium-binding polymer to normalize hyperkalemia. Initial targeted patients include those with chronic kidney disease (CKD) and heart failure (HF) for which the standard-of-care, renin-angiotensin-aldosterone system inhibitors (RAASi), can also cause life-threatening hyperkalemia. The company expects to file an NDA for patiromer in Q3:14 and we estimate U.S. launch in Q4:15.
- **Patiromer has shown a potentially best-in-class profile for the treatment of hyperkalemia, and we believe can achieve peak annual sales of about $1.4 billion in the U.S.** In the successful Phase 2b and Phase 3 trials, patiromer was shown to be effective at lowering serum potassium levels into the normal range, while also reducing the incidence of recurrent hyperkalemia with chronic dosing. We believe there is a significant patient need for a drug like patiromer as it would allow more CKD and HF patients to remain on RAASi therapies, which are highly effective, but can also cause hyperkalemia. In the U.S., we estimate there are about 2.4 million CKD and HF patients who would be immediately eligible for patiromer treatment with additional opportunities to further expand and grow the market. With a small specialty sales force of about 100 reps, we project peak annual sales of patiromer could reach about $1.4 billion in the U.S. alone.
- **We project cash runway through Q1:15 and potential full-year profitability in 2018.** Along the way, we anticipate data from the Phase 1 onset-of-action trial in H1:14 which would be supportive of a potential NDA filing in Q3:14. We estimate a FDA advisory committee (if necessary) would occur in Q2:15, followed by potential approval in Q3:15 and U.S. launch in Q4:15.
- **In our view, RLYP currently trading at about $20 per share or about $580 million market cap is at an attractive valuation compared to our fair value of $34 per share or about $1.2 billion market cap.** Our fair value is based on the sum of a 30% annual discount and a 1x-10x premium range on our net peak annual sales estimate for each product and indication in the clinic.

FYE Dec	2012A	2013E			2014E		
REV (M)	ACTUAL	CURR.	PREV.	CONS.	CURR.	PREV.	CONS.
Q1 Mar	--	$0.0A		--	$0.0E		--
Q2 Jun	--	0.0A		--	0.0E		--
Q3 Sep	--	0.0A		--	0.0E		--
Q4 Dec	--	0.0E		--	0.0E		--
Year*	**$0.0A**	**$0.0E**		**--**	**$0.0E**		**--**
Change	--	--			--		
	2012A	2013E			2014E		
EPS	ACTUAL	CURR.	PREV.	CONS.	CURR.	PREV.	CONS.
Q1 Mar	--	$(4.92)A		--	$(0.53)E		--
Q2 Jun	--	(3.78)A		--	(0.44)E		--
Q3 Sep	--	(1.30)A		--	(0.31)E		--
Q4 Dec	--	(0.76)E		--	(0.38)E		--
Year*	**$(8.36)A**	**($10.76)E**		**--**	**($1.65)E**		**--**
P/E	--	--			--		
Change	--	--			--		

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

December 9, 2013

Price
$19.99

Rating
OUTPERFORM

Fair Value Estimate
$34

Liana Moussatos, Ph.D.
(415) 263-6626
liana.moussatos@wedbush.com

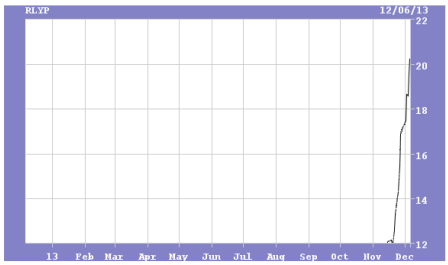
Richard Lau, CFA
(415) 274-6851
richard.lau@wedbush.com

Company Information

Shares Outst (M)	28.7
Market Cap (M)	$574
52-Wk Range	$11.90 - $21.40
Book Value/sh	$0.74
Cash/sh	$2.87
Enterprise Value (M)	$635
LT Debt/Cap %	21

Company Description

Relypsa is an emerging pharmaceutical company focused on the development and commercialization of treatments for renal, cardiovascular, and metabolic disorders. Patiromer, a non-absorbed polymer, is the lead drug candidate and is for the treatment of hyperkalemia.



Source: Thomson Reuters

Wedbush Securities does and seeks to do business with companies covered in its research reports. Thus, investors should be aware that the firm may have a conflict of interest that could affect the objectivity of this report. Investors should consider this report as only a single factor in making their investment decision. Please see page 19 of this report for analyst certification and important disclosure information.

Table of Contents

Investment Thesis

Relypsa is an emerging pharmaceutical company focused on the development and commercialization of cutting-edge treatments for renal, cardiovascular, and metabolic disorders. Its polymer drug discovery platform was in-licensed from Ilypsa, Inc., a subsidiary of Amgen (AMGN). Patiromer is the lead drug candidate emerging from this platform and is a non-absorbed, optimized potassium-binding polymer which is dosed twice daily as an oral suspension powder to normalize hyperkalemia in patients with chronic kidney disease (CKD) and/or heart failure (HF). Hyperkalemia (HK), a chronic condition characterized by excessive potassium, typically occurs in CKD and HF patients due to the body's inability to properly clear potassium. Furthermore, renin-angiotensin-aldosterone system inhibitors (RAASi), the standard-of-care for CKD and HF, can actually cause hyperkalemia themselves. Due to the lack of effective, safe, and tolerable treatments for hyperkalemia, treatment guidelines recommend reducing or discontinuing RAASi therapy if hyperkalemia develops—despite their protective effects on the kidney. This situation has created an unmet medical need for CKD and HF patients. In our view, patiromer has the potential to be best-in-class and the first breakthrough treatment for hyperkalemia since 1958. Compared to the only currently approved treatment for hyperkalemia, Kayexalate (an absorbed polymer), the physical and chemical properties of patiromer confer several advantages, including better binding capacity, tolerability and compliance. In fact, Kayexalate has never shown statistically significant reductions in serum potassium levels in prospective clinical trials. In addition, its poor tolerability profile makes it unsuitable for chronic administration. In contrast, patiromer was shown to be effective at lowering serum potassium levels into the normal range while also reducing the incidence of recurrent hyperkalemia with chronic dosing in the Phase 3 and Phase 2b programs. Given the clinical profile of patiromer, we believe it has the potential to fill an unmet need for CKD and HF patients with mild or moderate-to-severe hyperkalemia as well those on a suboptimal dose of a RAASi due to recurrent hyperkalemia. In the U.S., we estimate there are about 2.4 million CKD and HF patients who would be immediately eligible for patiromer treatment, with additional opportunities to further expand and grow the market. We anticipate the company will file an NDA in Q3:14, setting the stage for potential approval and launch in H2:15. With a small specialty sales force of about 100 reps, we project peak annual sales of patiromer could reach about $1.4 billion in the U.S. alone.

Key Points

1. **Relypsa is an emerging biopharmaceutical company developing non-absorbed polymer drug candidates to treat renal, cardiovascular and metabolic diseases.** Its polymer drug discovery platform was in-licensed from Ilypsa, Inc., a subsidiary of Amgen (AMGN). Patiromer is the lead drug candidate emerging from this platform and is a non-absorbed, optimized potassium-binding polymer which is dosed twice daily as an oral suspension powder to normalize hyperkalemia in patients who can benefit from treatment with renin-angiotensin-aldosterone system (RAAS) inhibitors—recommended for treatment of chronic kidney disease (CKD) and heart failure (HF)–but can also cause life-threatening hyperkalemia. Current treatments for hyperkalemia include dietary potassium restriction, potassium-wasting diuretics, or sodium polystyrene sulfonate (SPS/Kayexalate). These treatments have limited efficacy and tolerability issues which can become life-threatening—limiting their use for chronic daily administration. Patiromer's relatively high efficacy and benign side-effect profile is likely to make it best-in-class for chronic treatment of hyperkalemia, in our view. Behind patiromer, the company also has a preclinical-stage polymeric drug candidate, RLY6002, which is being developed as a pioneering approach to improve glycemic control in adults with type 2 diabetes.
2. **Relypsa's lead drug candidate, patiromer, has shown a potentially best-in-class profile in the successful pivotal Phase 3 and Phase 2b programs.** Results from Part A of the trial showed a mean reduction in serum potassium from baseline to week 4 of 1.01 mEq/L ($p < 0.001$; 95% CI -1.07, -0.95), with 76% of patients having normal serum potassium levels. After controlling serum potassium in Part A, patients were randomized to either continue on patiromer or switch to placebo in Part B. The difference between the placebo and patiromer groups in the median change in serum potassium from Part B baseline was 0.72 mEq/L ($p < 0.001$; 95% CI 0.46, 0.97). Given these statistically significant results and the fact that the Phase 3 study was conducted under a special protocol assessment (SPA), we believe FDA approval is likely. Furthermore, these results are supported by 52-week data from the Phase 2b trial which showed that chronic dosing with patiromer reduces the recurrence of hyperkalemia. To put all of these results in perspective, the only currently approved product for hyperkalemia, Kayexalate, has never shown statistically significant reductions in serum potassium levels in prospective clinical trials. In addition, its poor tolerability profile makes it unsuitable for chronic administration.
3. **Due to the potential for a best-in-class profile as well as the unmeet need for an efficacious hyperkalemia treatment suitable for chronic dosing, we believe commercial risks are reduced and project patiromer can achieve peak annual sales of about $1.4 billion in the U.S.** Hyperkalemia, a chronic condition characterized by excessive potassium, is often associated with chronic kidney disease (CKD) and heart failure (HF). Furthermore, renin-angiotensin-aldosterone system (RAAS) inhibitors which are commonly prescribed to treat these conditions can also cause hyperkalemia. Due to the lack of effective, safe, and tolerable treatments for hyperkalemia, treatment guidelines recommend reducing or discontinuing RAAS inhibitor therapy if hyperkalemia develops—despite their protective effects on the kidney. This situation has created an unmet medical need for CKD and HF patients, given Kayexalate is only suitable for acute dosing while RAASi therapy is needed chronically. In the U.S., we estimate there are about 2.4 million CKD and HF patients who would be immediately eligible for patiromer treatment with additional opportunities to further expand and grow the market. With a small specialty sales force of about 100 reps, we project peak annual sales of patiromer could reach about $1.4 billion in the U.S. alone.

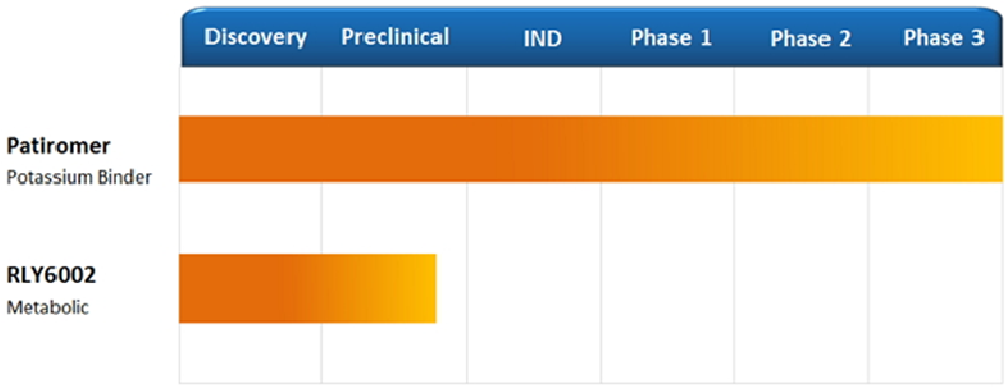
4. **We project cash runway through Q1:15 and potential full-year profitability in 2018.** The company ended Q3:13 with about $16.5 million in cash, investments, and equivalents. With net proceeds of approximately $77.9 million from the initial public offering (IPO), we project cash runway through Q1:15. Along the way, we anticipate data from the Phase 1 onset-of-action trial in H1:14 which would be supportive of a potential NDA filing in Q3:14. We estimate a FDA advisory committee (if necessary) would occur in Q2:15, followed by potential approval in Q3:15 and U.S. launch in Q4:15.
5. **We believe execution risk is reduced by management's quality and experience.** John Orwin is CEO and brings almost 25 years of experience in the pharmaceutical industry, most recently as CEO of Affymax. Given that the key driver for Relypsa will be approval and commercialization of patiromer, we believe Mr. Orwin's previous experience as senior vice president of the BioOncology Business Unit at Genentech where he was responsible for all marketing, sales, business unit operations and pipeline brand management for Genentech's oncology portfolio in the United States is very applicable. In addition to the CEO's extensive commercial experience, he is also surrounded by an impressive management team who we believe reduce execution risk.
6. **We consider intellectual property around patiromer to be strong due to multiple patents, including composition of matter, expiring in 2030 and beyond.** The company has been granted composition of matter and method of use patents in North America (US, CA, MX), Europe (UK, DE, NL, FR, IT), Asia (JP, CN, KR) and select other countries. In our view, the key U.S. patent protecting patiromer is No. 8,337,824 which covers "pharmaceutical composition of patiromer with a Ca-sorbitol counterion" and expires on May 29, 2030. Patiromer is also covered by numerous ex-U.S. patents which are expected to provide coverage through 2029.
7. **In our view, RLYP currently trading at about $20 per share or about $580 million market cap is at an attractive valuation compared to our fair value of $34 per share or about $1.2 billion market cap.** Based on the sum of a 30% annual discount and a 1x-10x premium range on our net peak annual sales estimate for each product and indication in the clinic, we calculate RLYP's current fair value at about $34 per share. Furthermore, with a CKD prevalence of about 8-16% of the worldwide population, we project patiromer could achieve blockbuster sales and make Relypsa a potential acquisition target. We project a current acquisition value at about $1.3 billion market cap or $36 per share for RLYP.

Relypsa's Drug Pipeline

RELYPSA'S PATIROMER HAS SHOWN POTENTIAL FOR BEST-IN-CLASS TREATMENT OF HYPERKALEMIA.

Patiromer is a non-absorbed, potassium-binding polymer that is specifically designed to bind and remove potassium from the GI tract, particularly the colon. Compared to the only currently approved treatment for hyperkalemia, Kayexalate (an absorbed polymer), the physical and chemical properties of patiromer confer several advantages, including better binding capacity, tolerability and compliance. In the two-part, pivotal Phase 3 study, patiromer was shown to effectively lower serum potassium levels into the normal range while also reducing the incidence of recurrent hyperkalemia. The company is in the process of completing CMC activities, as well as a supportive Phase 1 onset-of-action study and plans to submit an NDA in Q3:14. RLY6002 is a preclinical candidate and is being developed as a pioneering adjunct to diet and exercise to improve glycemic control in adult type 2 diabetics. Although Relypsa has a clinical development plan, it does not plan to further develop RLY6002 at this time as it devotes its resources to patiromer.

Figure 1: PIPELINE—BEST-IN-CLASS



Source: Company reports and Wedbush Pacgrow Life Sciences

Model, Valuation and Risks

WE PROJECT FULL-YEAR PROFITABILITY IN 2018 AFTER U.S. LAUNCH OF PATIROMER IN Q4 2015

The company plans to submit an NDA for patiromer in Q3:14 following completion of various CMC activities as well as a Phase 1 onset-of-action trial in H1:14. We anticipate a potential FDA advisory committee meeting (if necessary) in Q2:15, potential approval in Q3:15, and U.S. launch in Q4:15. In the U.S., we estimate there are about 2.4 million CKD and HF patients with moderate-to-severe hyperkalemia who would be immediately eligible for patiromer treatment with additional opportunities to further expand and grow the market. With a small specialty sales force of about 100 reps, we project peak annual sales of patiromer could reach about $1.4 billion in the U.S. alone. We believe upside to our estimates could come from greater-than-anticipated patiromer use in milder hyperkalemia patients along with those patients not currently on a RAASi or on a suboptimal RAASi dose. Furthermore, we have chosen to be conservative and not included any ex-U.S. sales in our model. The company ended Q3:13 with about $16.5 million in cash, investments, and equivalents. With net proceeds of approximately $77.9 million from the initial public offering (IPO), we project cash runway through Q1:15. Therefore, we anticipate the company may need additional capital in order to reach full-year profitability, which we model to occur in 2018.

FIGURE 2: MODEL—WE PROJECT FULL-YEAR PROFITABILITY IN 2018

Relypsa, Inc. (RLYP:NASDAQ)							**Wedbush Securities, Inc.**
Historical and Projected Income Statement							***Liana Moussatos, PhD***
(In thousands except per share data)							***Richard Lau***
	2012A	**2013E**	**2014E**	**2015E**	**2016E**	**2017E**	**2018E**
	FY:12A	**FY:13E**	**FY:14E**	**FY:15E**	**FY:16E**	**FY:17E**	**FY:18E**
Revenues:							
Patiromer	**-**	**-**	**-**	**6,506**	**81,088**	**237,994**	**565,023**
Total Net Product Revenues	$ -	$ -	$ -	$ 6,506	$ 81,088	$ 237,994	$ 565,023
Grant Revenue	-	-	-	-	-	-	-
Collaborative Licensing and Development Revenue	-	-	-	-	-	-	-
Total Revenues	**$ -**	**$ -**	**$ -**	**$ 6,506**	**$ 81,088**	**$ 237,994**	**$ 565,023**
Total COGS	-	-	-	5,205	57,915	141,711	270,048
Gross Margin	**$ -**	**$ -**	**$ -**	**$ 1,301**	**$ 23,173**	**$ 96,283**	**$ 294,975**
Operating Expenses:							
R&D	36,052	62,889	28,607	19,375	20,972	22,701	24,601
SG&A	7,285	12,226	18,477	44,499	63,699	66,285	68,977
Acquired in-process R&D	-	-	-	-	-	-	-
Total Operating Expenses	**$ 43,337**	**$ 75,115**	**$ 47,085**	**$ 63,874**	**$ 84,671**	**$ 88,987**	**$ 93,578**
Operating Income (Loss)	**(43,337)**	**(75,115)**	**(47,085)**	**(62,573)**	**(61,498)**	**7,296**	**201,397**
Interest Income / (Expense), net	(382)	(15,069)	(1,042)	(607)	(340)	(396)	(245)
Other Income / (Expense), net	(6)	(1,395)	(1,453)	(1,459)	(1,460)	(1,460)	(1,459)
Income Before Income Taxes	**$ (43,725)**	**$ (91,578)**	**$ (49,580)**	**$ (64,639)**	**$ (63,298)**	**$ 5,440**	**$ 199,693**
(Provision)/benefit for Income Taxes	-	-	-	-	-	(889)	(55,355)
Tax Rate	0.0%	0.0%	0.0%	0.0%	0.0%	2.5%	22.0%
Net Income (Loss)	**$ (43,725)**	**$ (91,578)**	**$ (49,580)**	**$ (64,639)**	**$ (63,298)**	**$ 4,551**	**$ 144,338**
GAAP EPS	**$ (8.36)**	**$ (10.76)**	**$ (1.65)**	**$ (2.11)**	**$ (2.03)**	**$ 0.14**	**$ 4.44**
Weighted Average Shares Outstanding	5,228	14,028	30,067	30,667	31,267	31,867	32,467
Cash	**$54,355**	**$73,848**	**$25,222**	**($57,672)**	**($151,136)**	**($162,227)**	**($34,064)**
Cash Per Share		**$5.26**	**$0.84**	**($1.88)**	**($4.83)**	**($5.09)**	**($1.05)**
Net Cash	**$54,355**	**$ 29,714**	**$ (18,912)**	**$ (101,806)**	**$ (195,270)**	**$ (206,361)**	**$ (78,198)**
Net Cash Per Share	**$10.40**	**$2.12**	**($0.63)**	**($3.32)**	**($6.25)**	**($6.48)**	**($2.41)**
Cash Burn (Generation)		**$17,307**	**$85,426**	**$119,694**	**$130,264**	**$47,891**	**($91,363)**

Sources: Company reports and Wedbush Pacgrow Life Sciences

In our view, RLYP currently trading at about $20 per share or about $580 million market cap is at an attractive valuation compared to our fair value of $34 per share, or about $1.2 billion market cap. Based on the sum of a 30% annual discount and a 1x-10x premium range on our net peak annual sales estimate for each product and indication in the clinic, we calculate RLYP's current fair value at about $34 per share. Furthermore, with a CKD prevalence of about 8-16% of the worldwide population, we project patiromer could achieve blockbuster sales and make Relypsa a potential acquisition target. We project a current acquisition

value at about $1.3 billion market cap or $36 per share for RLYP.

Figure 3: RLYP FAIR VALUE—$34 PER SHARE OR $1.2 BILLION MARKET CAPITALIZATION

RLYP Product Pipeline Valuation		Eligible #	Pricing	Gross Peak Sales	Net Peak Revs	Peak		Estimated/Actual	Discount	Estimate	Fair Value
Product	Indication	Patients	$/Patient	($000)	($000)	Penetration	Multiple	Launch	Rate	Fair Value	per Share
Patiromer (US)	Hyperkalemia (moderate to severe)	3,790,000	$6,120	$1,043,766	$1,043,766	15%	7	11/4/2015	30%	$918,503	$26.27
Patiromer (US)	Hyperkalemia (mild / suboptimal RAASi)	13,760,000	$6,120	$419,159	$419,159	2%	7	11/4/2015	30%	$283,735	$8.11
Patiromer (EU)	Hyperkalemia (moderate to severe)	2,526,667	$4,896	$402,043	$80,409	10%	7	11/3/2016	30%	$41,869	$1.20
Patiromer (EU)	Hyperkalemia (mild / suboptimal RAASi)	9,173,333	$4,896	$161,454	$32,291	1%	7	11/3/2016	30%	$12,934	$0.37
Patiromer (ROW)	Hyperkalemia (moderate to severe)	2,526,667	$3,917	$222,670	$22,267	8%	7	11/3/2017	30%	$8,919	$0.26
Patiromer (ROW)	Hyperkalemia (mild / suboptimal RAASi)	9,173,333	$3,917	$89,421	$8,942	1%	7	11/3/2017	30%	$2,755	$0.08
RLY-6002	T2D	139,900,146	$1,446	$1,154,672	$540,678	1%	1	1/2/2024	30%	$7,975	$0.23
We use multiples to account for clinical and regulatory risk at various stages of development.								Stock	MktCap		Upside
1: in preclinical testing	6: in Phase 3						Fair Value	$34.38	$1,202,237		72%
2: passed preclinical	7: Phase 3 data						Total Pipeline Value	$36.51	$1,276,689		
3: IND filing/stable mature product	8: regulatory review						Current Cash	$2.11	$73,848		
4: Phase 1 data	9: approved						Current Price	$19.99	$572,436		
5: Phase 2 data	10: launched										

Source: Company data, Wedbush Securities, Inc.

Risks to attainment of our fair value include: 1) Clinical – There is risk that results from the ongoing Phase 1 onset-of-action study are negative, but we view this is unlikely.; 2) Regulatory – Although the Phase 3 program was successful and conducted under a special protocol assessment (SPA), the FDA may fail to approve patiromer in a timely fashion, if at all.; 3) Manufacturing – Relypsa relies on third party suppliers to manufacture patiromer and there is risk that those parties may not meet their obligations. In addition, they may not be able to successfully scale up manufacturing in a timely and cost efficient manner.; 4) Commercial – As with all new product launches, initial sales of patiromer could be slower than anticipated and call into question its ultimate sales potential. Furthermore, patiromer could face competition from potential new drugs for hyperkalemia including ZS Pharma's late-stage candidate, ZS-9.; 5) Financing – The company ended Q3:13 with about $16.5 million in cash, investments, and equivalents. With net proceeds of approximately $77.9 million from the initial public offering (IPO), we project cash runway through Q1:15. Therefore, Relypsa will likely need to raise additional funds in order to commercially launch patiromer and to ultimately reach profitability which we model to occur in 2018.

Upcoming Catalysts

Next: We anticipate data from the Phase 1 onset-of-action trial in H1:14, which would be supportive of a potential NDA filing in Q3:14. We estimate a FDA advisory committee (if necessary) would occur in Q2:15, followed by potential approval in Q3:15 and U.S. launch in Q4:15.

Figure 4: ANTICIPATED MILESTONES (*our estimates)—TRANSFORMING IN 2014/2015

H1:14	PATIROMER PHASE 1 ONSET-OF-ACTION RESULTS
H1:14	COMPLETION OF CMC ACTIVITIES SUPPORTIVE OF NDA
Q3:14	**PATIROMER NDA SUBMISSION**
Q2:15	**POTENTIAL FDA ADVISORY COMMITTEE FOR PATIROMER**
Q3:15	**POTENTIAL FDA APPROVAL OF PATIROMER (*IF NECESSARY)**
Q4:15	**POTENTIAL U.S. LAUNCH OF PATIROMER**
2014/2015*	POTENTIAL PATIROMER PARTERSHIP(S)

Source: Company reports and Wedbush Pacgrow Life Sciences

Management Team

We believe execution risk is reduced by management's quality and experience. John Orwin is CEO and brings almost 25 years of experience in the pharmaceutical industry, most recently as CEO of Affymax. Given that the key driver for Relypsa will be approval and commercialization of patiromer, we believe Mr. Orwin's previous experience as senior vice president of the BioOncology Business Unit at Genentech where he was responsible for all marketing, sales, business unit operations and pipeline brand management for Genentech's oncology portfolio in the United States is very applicable. In addition to the CEO's extensive commercial experience, he is also surrounded by an impressive management team who we believe reduce execution risk.

FIGURE 5: RELYPSA MANAGEMENT—QUALITY AND EXPERIENCE REDUCES EXECUTION RISK, IN OUR VIEW

Name	Position and Past Experience
John Orwin	**President and Chief Executive Officer.** Mr. Orwin joined Relypsa in June of 2013 bringing nearly 25 years of experience in the biotechnology and pharmaceutical industries. Prior to Relypsa, Mr. Orwin served as chief executive officer and a member of Affymax's board of directors starting in February 2011. From April 2010 to January 2011, he served as president and chief operating officer of Affymax. From 2005 to 2010, Mr. Orwin served as vice president and then senior vice president, BioOncology Business Unit, at Genentech, where he was responsible for all marketing, sales, business unit operations and pipeline brand management for Genentech's oncology portfolio in the United States. From 2001 to 2005, Mr. Orwin served in various executive-level positions at Johnson & Johnson, overseeing oncology therapeutic commercial and portfolio expansion efforts in the US. He has also held senior marketing and sales positions at Alza Pharmaceuticals, Sangstat Medical Corporation, Rhone-Poulenc Rorer Pharmaceuticals and Schering-Plough Corporation. Mr. Orwin holds an M.B.A. from New York University and a B.A. from Rutgers University.
Kristine M. Ball	**Chief Financial Officer, SVP.** Ms. Ball joined Relypsa in November 2012 bringing almost 20 years' experience in the life sciences industry in both in-house and public accounting roles. Prior to Relypsa, Ms. Ball was senior vice president of finance and administration and chief financial officer of KAI Pharmaceuticals, Inc., a venture-backed drug discovery company acquired by Amgen, Inc. for $315 million. At KAI she was responsible for finance, administration and strategic planning, led a $35 million round of venture financing and was a key member of the deal teams responsible for two pharmaceutical partnerships and the Amgen acquisition. Prior to KAI, Ms. Ball served as vice president of finance at Exelixis, Inc., a publicly traded biotechnology company, where she was involved in four acquisitions and in raising over $360 million through the company's initial public offering and other financings. Prior to Exelixis, Ms. Ball was a senior manager in Ernst & Young's life sciences audit practice. Ms. Ball is a certified public accountant and holds a BS in accounting from Babson College.
Lance Berman, M.D., M.S.	**Chief Medical Officer, SVP.** Mr. Berman joined Relypsa in December 2011 as Senior Vice President, Commercial Strategy and Medical Affairs and was promoted in October 2012 to Senior Vice President and Chief Medical Officer. Most recently, he was Chief Medical Officer of CPEX Pharmaceuticals where he was responsible for the clinical development of the company's late stage clinical product as well as its in-licensing and acquisition strategies. Prior to that, he served in various medical leadership roles at Pfizer Inc. from June 2003 to January 2009, where he was responsible for atherosclerosis, hypertension and endocrinology products serving at various times as US or Global Medical Team Leader. Previously, Mr. Berman held roles of increasing responsibility at Schering-Plough Corporation (merged with Merck) and Janssen Pharmaceuticals, Inc. (Johnson & Johnson). Mr. Berman received his Bachelor of Medicine and Bachelor of Surgery at the University of Cape Town in Cape Town, South Africa, and holds a Masters Degree in Pharmaceutical Medicine.
Jerry Buysse, Ph.D.	**Chief Scientific Officer, SVP Research.** Mr. Buysse joined Relypsa in October 2007. Previously, he was Vice President of Preclinical Research and Development at Ilypsa, responsible for lead discovery, preclinical development and pharmacology. Mr. Buysse joined Ilypsa in May, 2003 following seven years at Microcide Pharmaceuticals where he was VP of Discovery Biology, responsible for screening and lead discovery in Microcide's antibacterial and antifungal programs. Mr. Buysse was a Senior Research Scientist at Pharmacia & Upjohn (1992-1996) and contributed to preclinical development of Linezolid (Zyvox). Jerry received his BS in Microbiology at The University of Michigan and Ph.D. in Immunology and Microbiology from The Wayne State University School of Medicine in Detroit, MI.
Jennifer Chung	**VP Commercial.** Ms. Chung joined Relypsa in February 2013 bringing nearly 20 years' experience in pharmaceutical marketing. Prior to Relypsa, Ms. Chung held multiple commercial leadership roles at Pfizer, developing and implementing marketing and sales strategies for over 7 major pharmaceutical brands and leading the commercial development of several phase 2-3 candidates in the Cardiovascular and Neuroscience arena. During her career at Pfizer, Ms. Chung held roles of increasing responsibility, leading teams in consumer, professional and managed care marketing for products in various lifecycle stages and revenue size ($2B to $100MM), in both US and global markets. Ms. Chung holds a Bachelor of Science in Pharmacy from Rutgers University College of Pharmacy and a Masters in

	Business Administration from Fordham University.
Claire Lockey	**SVP Pharmaceutical Development and Regulatory Affairs.** Ms. Lockey joined Relypsa in February 2010 with over 35 years of experience in the pharmaceutical industry. For over six years she was Vice President Regulatory Affairs at FibroGen, Inc. Prior to that Ms. Lockey held similar executive-level positions at other biopharmaceutical companies including Titan Pharmaceuticals, Layton Bioscience, Connetics, Gore Hybrid Technologies and a ten-year consulting position at Synergia, an organization focused on the regulatory and clinical development of new health care products. Ms. Lockey earned her B.A. in Biology at Boston University.
Wilhelm Stahl, Ph.D.	**SVP Pharmaceutical Operations.** Mr. Stahl joined Relypsa in September 2011. Previously, he was a Managing Partner of Rondaxe Enterprises, providing consulting services and strategic advice on CMC aspects of drug development, including supply chain management and strategic business support. Until 2008, he was Head of the Pharma Custom Manufacturing business of Saltigo GmbH, a subsidiary of Lanxess AG. Mr. Stahl began his career as a medicinal chemist with Hoechst AG and run HMR's global high throughput screening center. After moving to Bayer AG in 1999 as director of CNS discovery chemistry, he led Life Science Research in Central Research and advanced to become Head of Research and Development and Pharma Marketing and Sales for Bayer's Fine Chemicals Division and for Lanxess, after its spinout from Bayer. Mr. Stahl earned both his undergraduate and Ph.D. degrees from the Institute for Organic Chemistry and Biochemistry at the University of Bonn.
Ronald Krasnow, J.D.	**SVP General Counsel.** Mr. Krasnow joined Relypsa in October 2007 and now serves as Relypsa's General Counsel and Senior Vice President. Prior to Relypsa, Mr. Krasnow was at Symyx Technologies, Inc. where he spent 10 years in various positions, including Senior Vice President, Intellectual Property. Mr. Krasnow has also been a Patent Examiner at the US Patent and Trademark Office. Mr. Krasnow received his BS in Materials and Metallurgical Engineering from The University of Michigan and JD from The George Washington University Law School.

Sources: Company reports and Wedbush Pacgrow Life Sciences

Intellectual Property

Relypsa's intellectual property: Patiromer has composition-of-matter protection through 2030 in the U.S. The company has been granted composition of matter and method of use patents in North America (US, CA, MX), Europe (UK, DE, NL, FR, IT), Asia (JP, CN, KR) and selected other countries. In our view, the key U.S. patent protecting patiromer is No. 8,337,824 which covers "pharmaceutical composition of Patiromer with a Ca-sorbitol counterion" and expires on May 29, 2030. Patiromer is also covered by numerous ex-U.S. patents which are expected to provide coverage through 2029.

Ilypsa Licensing Agreement: Relypsa's polymer drug discovery technology was originally created and validated at Symyx Technologies, Inc. Symyx then licensed certain assets related to the discovery and development platform to Ilypsa, Inc., a biopharmaceutical company, acquired by Amgen in 2007. Following the acquisition, Relypsa and Ilypsa (Amgen) entered into an IP License Agreement that granted Relypsa an exclusive sublicense under patent rights originally licensed to Ilypsa for the development and commercialization of pharmaceutical products developed using the polymer-based technology. Under the terms of the agreement, Relypsa does not have any royalty obligations with respect to patiromer, and has already satisfied the $12.5 million milestone obligation upon dosing of the first patient in the Phase 3 trial. Although Relpysa is not currently developing any other products covered under the agreement, it would owe certain royalties on product sales other than patiromer. Additionally, in the event of a change of control, Relypsa would owe Ilypsa (Amgen) a percentage of the purchase price ranging from 6.7% to 10%, up to a maximum of $30 million.

FIGURE 6: INTELLECTUAL PROPERTY PROTECTION THROUGH 2030 IN THE U.S.

PRODUCT	Patent Number	Expiration	Claimed Subject Matter
Patiromer	7,556,799	2/27/2025	Method for removing potassium by administering Patiromer
	8,147,873	3/11/2026	Pharmaceutical composition of Patiromer in bead form
	8,216,560	3/14/2027	Method of removing potassium from a CKD or HF patient being treated with a RAAS agent by administering Patiromer
	8,282,913	3/11/2026	Pharmaceutical composition of Patiromer and excipient
	8,287,847	10/11/2025	Method of treating hyperkalemia by administering Patiromer
	8,337,824	5/29/2030	Pharmaceutical composition of Patiromer with a Casorbitol counterion

Sources: Company reports and Wedbush Pacgrow Life Sciences

Patiromer for Hyperkalemia

Summary. We believe patiromer has the potential to be best-in-class and the first breakthrough treatment for hyperkalemia since 1958. Patiromer is a non-absorbed, potassium-binding polymer that is specifically designed to bind and remove potassium from the GI tract, particularly the colon, while avoiding dietary potassium. Compared to the only currently approved treatment for hyperkalemia, Kayexalate (an absorbed polymer), the physical and chemical properties of patiromer confer several advantages including better binding capacity, tolerability and compliance. In fact, Kayexalate has never shown statistically significant reductions in serum potassium levels in prospective clinical trials. In addition, its poor tolerability profile makes it unsuitable for chronic administration. In contrast, patiromer was shown to be effective at lowering serum potassium levels into the normal range while also reducing the incidence of recurrent hyperkalemia with chronic dosing in the Phase 3 and Phase 2b programs.

Hyperkalemia (HK), a potentially life-threatening chronic condition characterized by excessive potassium, typically occurs in CKD and HF patients due to the body's inability to properly clear potassium. Furthermore, renin-angiotensin-aldosterone system inhibitors (RAASi), the very drugs used to treat CKD and HF, can actually cause hyperkalemia themselves. Due to the lack of effective, safe, and tolerable treatments for hyperkalemia, treatment guidelines recommend reducing or discontinuing RAASi therapy if hyperkalemia develops—despite protective effects on the kidney. This situation has created an unmet medical need for CKD and HF patients with mild or moderate-to-severe hyperkalemia as well those on a suboptimal dose of a RAASi due to recurrent hyperkalemia. In the U.S., we estimate there are about 2.4 million CKD and HF patients with moderate-to-severe hyperkalemia who would be immediately eligible for patiromer treatment with additional opportunities to further expand and grow the market. We anticipate the company will file an NDA in Q3:14, setting the stage for potential approval and launch in H2:15. With a small specialty sales force of about 100 reps, we project peak annual sales of patiromer could reach about $1.4 billion in the U.S. alone.

Disease and Treatment Background

UNMET NEED: HYPERKALEMIA ASSOCIATED WITH CHRONIC KIDNEY DISEASE, HEART FAILURE, AND RAASi TREATMENT

Hyperkalemia, a chronic condition which may have acute episodes, can lead to life-threatening cardiac arrhythmias and sudden death. The typical characterization is serum potassium above 5.0 milliequivalents per liter (mEq/L). Patients with moderate-to-severe hyperkalemia have serum potassium at or over 5.5 mEq/L and have a ten-fold increase in 24-hour mortality. Hyperkalemia can be associated with reduced kidney function, diabetes, soft tissue injury, age, high dietary potassium, and certain medications including renin-angiotensin-aldosterone system (RAAS) inhibitors. Patients with chronic kidney disease (CKD) who have decreased capacity to excrete potassium typically have hyperkalemia. Guidelines for treating CKD recommend RAAS inhibitors (RAASi) to preserve kidney function and delay progression to renal failure and end-stage renal disease (ESRD). However, RAASi's are also associated with hyperkalemia, which can limit their use. Patients with heart failure (HF) may also have hyperkalemia and RAASi's are also recommended to reduce mortality.

In the U.S., the treatments for hyperkalemia are insufficient and include restriction of dietary potassium and potassium-excreting diuretics such as Kayexalate (sodium polystyrene sulfonate with sorbitol) which was first introduced to the market in 1958 and is the only approved treatment for hyperkalemia. However, its chronic use is limited by serious gastrointestinal side effects and an unfavorable taste. Due to the lack of effective, safe, and tolerable treatments for hyperkalemia, treatment guidelines recommend reducing or discontinuing RAASi therapy if hyperkalemia develops—despite their protective effects on the kidney. This situation has created an unmet medical need for CKD and HF patients.

We are also aware of at least one potential competitor, ZS Pharma, who is developing ZS-9 for the treatment of hyperkalemia. ZS-9 is a zirconium silicate particle designed as a highly selective oral sorbent to trap potassium ions throughout the GI tract. ZS Pharma recently presented top-line results from a Phase 3 trial at the American Society of Nephrology (ASN) Scientific Meeting (Nov. 5 – 10, 2013; Atlanta, GA) and plans to announce additional results in the coming months. We are not aware of ZS Pharma's future development and regulatory plans, but we estimate ZS-9 is roughly about one year behind patiromer in development. Based on the public data available to date, we believe ZS-9 has demonstrated efficacy and safety in the acute (48 hours) setting, but has not yet been adequately tested for chronic administration. In our view, ZS-9 seems to be a promising candidate with questions remaining with regards to long-term efficacy and safety with repeat administration. With that being said, we believe that the market opportunity is more than large enough to ultimately support two products.

Market Opportunity and Commercialization

MARKET OPPORTUNITY: WE PROJECT PEAK ANNUAL SALES OF ABOUT $1.4 BILLION IN THE U.S.

We estimate about 2.4 million patients would be immediately eligible for patiromer treatment in the U.S. It is estimated that more than 20 million adults in the U.S., an incidence rate of about one in ten, have some level of CKD, according to the Centers for Disease Control and Prevention. In addition, it is estimated that about 5.7 million Americans have heart failure. Given the patient profile of the Phase 3 study, we believe the immediately addressable patient populations are Stage 3 and 4 CKD, or non-CKD HF patients with moderate to severe hyperkalemia (K+ ≥5.5 mEq/L). In the U.S., there are an estimated 3 million, 0.85 million and 3.7 million patients with CKD 3, CKD 4, and non-CKD HF, respectively. Of the CKD 3, CKD 4, and non-CKD HF patient groups, about 20%, 40%, and 23% have moderate-to-severe hyperkalemia, respectively. This adds up to about 3.8 million people in the U.S. and of those between 60-70% present to a nephrologist or cardiologist. We calculate an immediately addressable patient population for patiromer of about 2.4 million patients in the U.S. In our view, these are the low-hanging fruit for patiromer, while additional market opportunities exist.

In addition to the immediately addressable moderate to severe hyperkalemia patients, we also believe patiromer could be used in mild hyperkalemia patients, along with those patients not currently on a RAASi or on a suboptimal RAASi dose. According to market research conducted by Relypsa, about 40% of physicians indicated that they would likely intervene with treatment for mild hyperkalemia (K+ <5.5 mEq/L), particularly in those patients with recurrent episodes. Furthermore, patiromer could allow physicians to initiate or re-initiate RAASi therapy in their CKD and HF patients who are not currently on a RAASi due to hyperkalemia. In addition, a significant number of CKD and HF patients are currently on a sub-optimal RAASi dose due to the risk of hyperkalemia and we believe patiromer would allow these patients to titrate up to a more optimal dose.

The relatively small target audience of physician specialists can be adequately addressed with a specialty sales force of about 100 reps. Patients with CKD and/or HF are typically treated by nephrologists or cardiologists. Relypsa intends to target about 7,000 nephrologists and about 1,000 HF centers in the U.S. The company believes a specialty sales force of about 100 representatives can adequately cover this specialty audience. Because a significant number of hyperkalemia patients are also treated by primary care physicians, Relypsa may explore partnership(s) to target the primary care market. Furthermore, the company may seek one or more partner(s) to commercialize patiromer outside of the U.S.

Patiromer Properties

PATIROMER PHYSICAL AND CHEMICAL PROPERTIES: NUMEROUS A DVANTAGES COMPARED TO KAYEXALATE

Patiromer is a non-absorbed, potassium-binding polymer that is formulated as a dry, odorless powder and suspended in water for administration. It was specifically designed to bind and remove potassium from the GI tract, particularly the colon, while avoiding dietary potassium. Compared to Kayexalate (an absorbed polymer), patiromer's properties confer several advantages including better binding capacity, tolerability and compliance. In fact, Kayexalate has never shown statistically significant reductions in serum potassium levels in prospective clinical trials. In addition, its poor tolerability makes it unsuitable for chronic administration.

FIGURE 7: PATIROMER VS. KAYEXALATE

Property	Patiromer	Kayexalate
Chemistry and Binding	Small MW K+ binding units, synthesized by suspension polymerization process, significant K+ binding capacity (in vitro)	Large MW K+ binding units, synthesized by bulk polymerization process, moderate K+ binding capacity (in vitro)
Design/API	Spheres of uniform size, free-flowing polymer beads	Irregular bulk gel material, sharp edges, non-uniform size and fines, clay-like consistency
Counterion	Ca^{2+}/sorbitol-loaded	NA^{+}-loaded, causes risk of fluid retention and/or hypertension
Efficacy	8 clinical studies with proven K+ reduction and control	No published efficacy data from prospective clinical trials (approval grandfathered in)
Safety and Tolerability	Non-absorbed, well-tolerated	Intestinal necrosis warning GI side effects
Dosing/Compliance	Lower dose, neutral taste	Gritty, unpleasant taste, up to 60g TID

Sources: Company reports and Wedbush Pacgrow Life Sciences

Patiromer Development Background and Current Status

WE ANTICIPATE NDA SUBMISSION IN Q3:14 AND POTENTIAL U.S. LAUNCH IN Q4:15.

The company plans to submit an NDA for patiromer for the treatment of hyperkalemia in Q3:14. The basis of the NDA will include the pivotal Phase 3 trial (RLY5016-301), the long-term treatment Phase 2b trial (RLY5016-205) and the Phase 1 onset-of-action trial (RLY5016-103). Both the Phase 3 and Phase 2b trials have been completed, while the Phase 1 trial is ongoing with data expected in H1:14. Importantly, the pivotal Phase 3 trial was conducted under a Special Protocol Assessment (SPA) agreed to by the FDA. We anticipate a potential FDA advisory committee meeting (if necessary) in Q2:15, potential approval in Q3:15, and U.S. launch in Q4:15.

In addition to the clinical data, Relypsa has also completed extensive nonclinical toxicology work. Long-term chronic exposure of patiromer in various animal models demonstrated that it was not associated with adverse effects or abnormal pathology at doses up to 15 times the maximum human daily dose. In addition, preclinical safety data showed that patiromer was not genotoxic and was not associated with adverse effects in cardiovascular, central nervous system, gastrointestinal motility or pulmonary safety pharmacology studies. Patiromer was also shown to be non-absorbed from the intestinal tract and drug-drug interaction studies indicated it does not interfere with common drugs used in the target patient population.

The company is targeting a label that indicates patiromer for the treatment of hyperkalemia in any patient with high potassium levels (above upper limit of normal), irrespective of the cause. The intended dosage and administration will recommend a starting dose of 8.4 g/day or 16.8 g/day administered orally as a divided dose twice a day.

From a manufacturing standpoint, the company is conducting 36-month stability studies and the 18-month data needed for NDA filing is expected in H1:14. Relypsa believes that these data will support the storage of patiromer for 12 to 15 months at 2° to 8°C and up to 3 to 6 months at 25°C. By H1:14, they also plan to complete various other Chemistry, Manufacturing, and Controls (CMC) activities needed for NDA filing.

PATIROMER HAS BEEN TESTED IN EIGHT CLINICAL TRIALS INCLUDING A PIVOTAL PHASE 3 STUDY

FIGURE 8: PHASE 3 STUDY DESIGN

Patiromer Clinical Development				
Trial	**Status**	**Subjects (active/ placebo)**	**Objectives**	**Selected Results**
Phase 1 Trials				
RLY5016-101	Completed	33 (25/8)	Safety and tolerability of single and multiple doses of patiromer. Effects on urinary and fecal potassium excretion.	• Significant dose-dependent increase in fecal potassium excretion at doses of 15–60 grams/day compared with placebo. • Corresponding decrease in urinary potassium excretion. • Well-tolerated.
RLY5016-102	Completed	12 (12/0)	Pharmacological activity/safety of TID, BID and QD dosing of patiromer.	• Significant increase in fecal potassium excretion and a concomitant decrease in urinary potassium excretion across the QD/BID/TID dosing regimen.
RLY5016-103	Ongoing	15 (15/0)	Time to onset of potassium-lowering action in subjects with CKD and hyperkalemia.	• Results expected first half of 2014.
Phase 2a Proof-of-Concept Trial				
RLY5016-201	Completed	6 (6/0)	Efficacy/safety of a fixed-dose of patiromer in subjects with hyperkalemia despite receiving hemodialysis 3 times weekly.	• Patiromer was pharmacologically active in reducing serum potassium levels and was well-tolerated.
Phase 2 Prevention Trials				
RLY5016-202 (PEARL-HF)	Completed	105 (56/49)	Efficacy/safety in preventing hyperkalemia in HF patients on a RAAS inhibitor.	• Statistically significant difference in mean serum potassium levels for those subjects on patiromer versus placebo. • Patiromer reduced incidence of hyperkalemia. • A significantly greater percentage of HF subjects on patiromer were able to increase the dose of the spironolactone compared to subjects on placebo.
RLY5016-204	Completed	63 (63/0)	Efficacy/safety of a titration regimen in preventing hyperkalemia in subjects with HF and CKD on a RAAS inhibitor.	• When titrated, patiromer provided reliable control of serum potassium levels in over 90% of subjects.
Phase 2b Treatment Trial				
RLY5016-205 (AMETHYST-DN)	Completed	306 (306/0)	• Efficacy/safety in treating hyperkalemia in CKD patients. • Determination of starting dose. • Long-term safety in chronic treatment.	Treatment Initiation Period: • Met primary endpoint, statistically significant reduction in mean serum potassium at week 4. Long-term Maintenance Period: • Significant majority of subjects in normal range at 52 weeks.
Pivotal Phase 3 Trial				
RY5016-301	Completed	Part A: (243/0) Part B: 107 (55/52)	Part A: To evaluate the efficacy and safety of patiromer for the treatment of hyperkalemia. Part B: • To evaluate the effect of withdrawing patiromer on control of serum potassium levels. • To assess whether chronic treatment with patiromer prevents the recurrence of hyperkalemia. • To provide placebo-controlled safety data.	Part A: • Met primary endpoint: statistically significant reduction in mean serum potassium at week 4. Part B: • Met primary endpoint: Statistically significant difference between patiromer and placebo in the change from baseline in serum potassium. • Met secondary endpoints: Significantly higher recurrence of hyperkalemia, after being controlled in Part A, in placebo as compared to patiromer.

Sources: Company reports and Wedbush Pacgrow Life Sciences

Clinical History

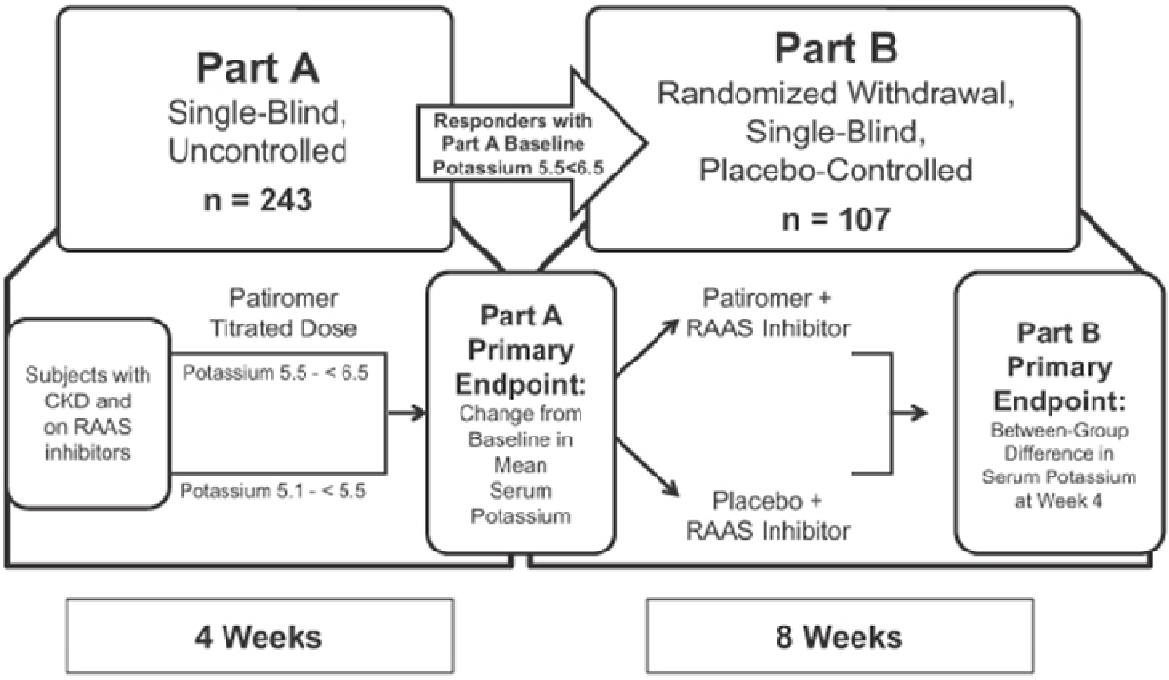
PIVOTAL PHASE 3 STUDY (RLY5016-301)

Phase 3 Study Design. RLY5016-301 is a two-part, pivotal Phase 3 study that was conducted under a Special Protocol Assessment (SPA). The two parts of the study will each serve as a pivotal trial.

Part A: The first part of the study was a 4-week, single arm, single-blind trial that enrolled 240 subjects. Patients with a baseline serum potassium level of 5.1 to <5.5 mEq/L were placed into Dose Group 1 while patients with baseline serum potassium of 5.5 to ≤6.5 mEq/L were place into Dose Group 2. Because patients entering the study were hyperkalemic, it was deemed unethical to use a placebo control arm in Part A. The primary endpoint for Part A was the change from baseline to week 4 in mean serum potassium levels with a target reduction of at least 0.7 mEq/L ($p<0.05$) considered to be clinically meaningful by the FDA.

Part B: The second part of the study was an 8-week, parallel group, single-blind placebo-controlled randomized withdrawal trial that enrolled 80 subjects. Patients from Part A with a baseline serum potassium level ≥5.5 mEq/L and who were defined as responders at the end of Part A were eligible to be randomized into Part B. In the event of recurrent hyperkalemia, patients in the patiromer group increased their patiromer dose, while patients in the placebo group decreased their RAASi dose. The primary endpoint for Part B was the difference between the patiromer and placebo groups in the change in serum potassium levels.

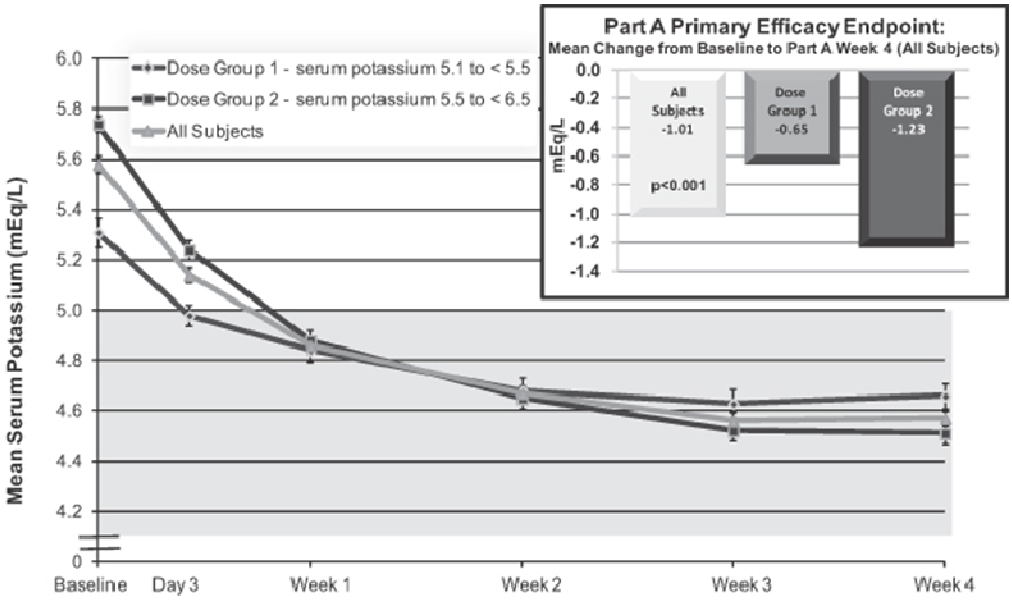
FIGURE 9: PHASE 3 STUDY DESIGN



Sources: Company reports and Wedbush Pacgrow Life Sciences

Part A Results: Both the primary and secondary efficacy endpoints were achieved. The change in serum potassium from baseline to week 4 was a reduction of 1.01 mEq/L ($p < 0.001$; 95% CI -1.07, -0.95). Broken down by dose group, the reduction was 0.65 mEq/L ($p < 0.05$; 95% CI -0.74, -0.55) and 1.23 mEq/L ($p < 0.05$; 95% CI -1.31, -1.16) in Dose Group 1 and Dose Group 2, respectively. The proportion of subjects with serum potassium in the target range of 3.8 to < 5.1 mEq/L (normal range) at week 4 (secondary endpoint) was 76% ($p < 0.05$; 95 CI 70, 81). Adverse events (AE) were reported by 44% of subjects with the most common being mild-to-moderate gastrointestinal (GI) symptoms (19%). Importantly, there were no severe GI events, and thus, we view patiromer's tolerability profile as favorable. There were four serious adverse events (SAEs) and all four were independently assessed as unrelated to patiromer. The four events were paroxysmal atrial fibrillation with tachyarrhythmia, a urinary tract infection with bacteremia and sub-therapeutic anticoagulant blood levels, and in the same subject, after study discontinuation, endocarditis, and worsening renal function. Although mean serum magnesium levels remained in the normal range, 3% of subjects developed hypomagnesium with the lowest reported level being 1.2 mg/dL (classified as Grade 1). Although hypomagnesium is a theoretical safety concern for patiromer, we don't believe these data are alarming.

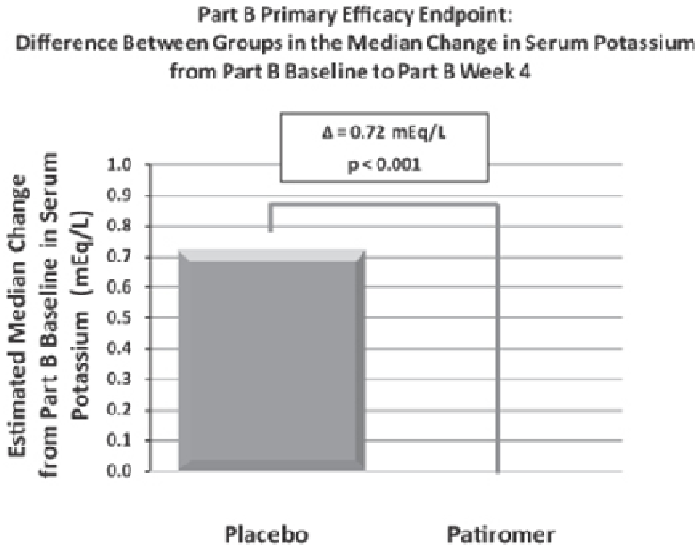
FIGURE 10: PHASE 3 PART A RESULTS

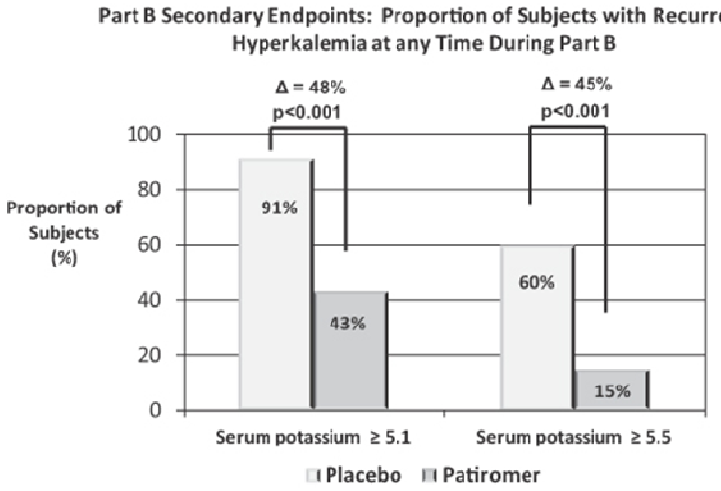


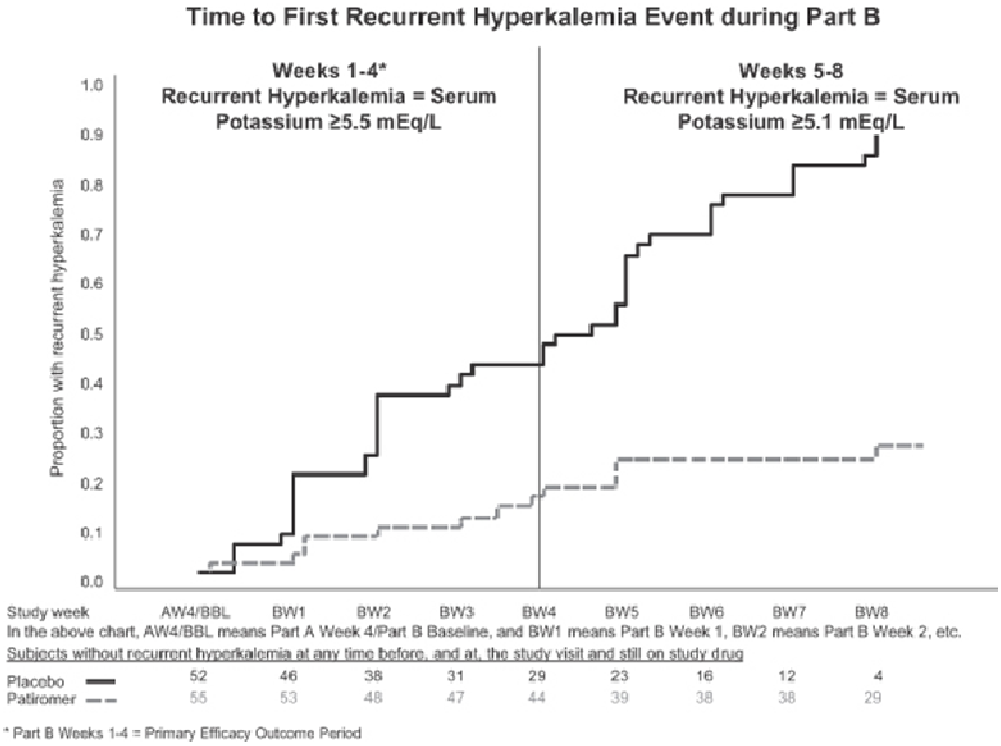
Sources: Company reports and Wedbush Pacgrow Life Sciences

Part B Results: Both the primary and secondary efficacy endpoints were achieved. The difference between the placebo and patiromer groups in the median change in serum potassium from Part B baseline was 0.72 mEq/L ($p < 0.001$; 95% CI 0.46, 0.97). The two secondary endpoints which evaluated the proportion of subjects who developed recurrent hyperkalemia after having been controlled in patiromer in Part A were also successful. When recurrent hyperkalemia was defined as serum potassium ≥ 5.1 mEq/L, there was a 48% difference between groups in the proportion of patients (43% patiromer vs. 91% placebo) who developed recurrent hyperkalemia ($p < 0.001$; 95% CI 0.33, 0.63). When recurrent hyperkalemia was defined as serum potassium ≥ 5.5 mEq/L, there was a 45% difference between groups in the proportion of patients (15% patiromer vs. 60% placebo) who developed recurrent hyperkalemia ($p < 0.001$; 95% CI 0.33, 0.63). In addition, more patients in the placebo group developed recurrent hyperkalemia, and this occurred earlier and more rapidly compared to the patiromer group. A similar proportion of placebo (46%) and patiromer (46%) subjects reported at least one AE with a greater portion of patiromer subjects (13% patiromer vs. 6% placebo) reporting a GI AE. Importantly, there were no serious GI AEs reported by patiromer subjects. There was one SAE (fatal mesenteric artery and gallbladder artery thrombosis), but it was deemed unrelated to patiromer. Although mean serum magnesium levels remained in the normal range throughout Part B, 2% of subjects in each group developed hypomagnesemia, with no severe cases of hypomagneseia reported.

FIGURE 11: PHASE 3 PART B RESULTS





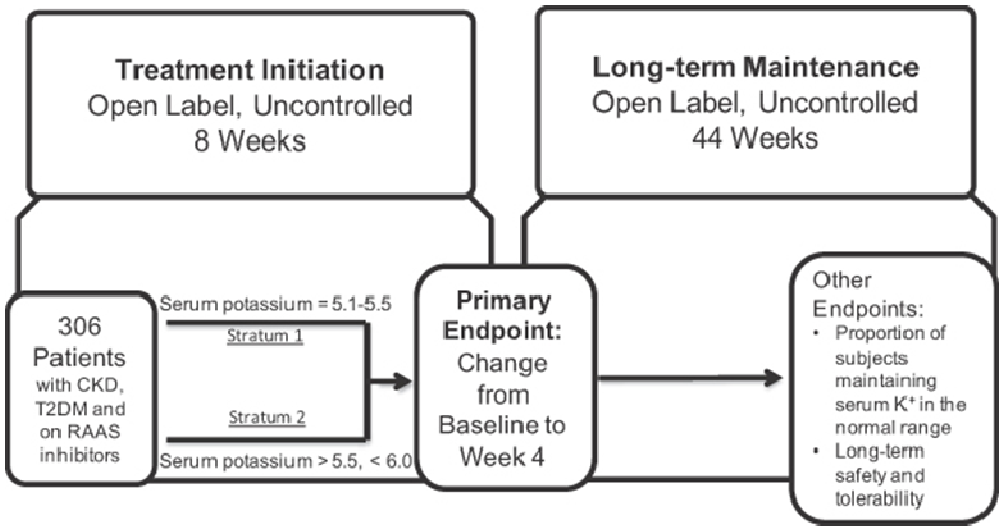


Sources: Company reports and Wedbush Pacgrow Life Sciences

PHASE 2B STUDY (RLY5016-205 AMETHYST-DN)

Phase 2b Study Design. AMETHYST-DN is an open-label, randomized, dose-ranging study that was conducted to determine the optimal starting dose, efficacy, and safety of patiromer in treating hyperkalemia. The trial had two treatment phases: 8-week treatment initiation and 44-week long-term maintenance. The trial enrolled 306 subjects with CKD and Type 2 diabetes, and on a RAAS inhibitor. Patients with baseline serum potassium levels from 5.1 to 5.5 mEq/L were assigned to Stratum 1, while those with levels from 5.5 mEq/L to 6.0 mEq/L were assigned to Stratum 2. Patients in each stratum received one of three starting doses and were titrated to an individual patiromer dose based on their serum potassium levels. All patients were eligible to roll into the maintenance phase and about 64% of subjects completed one year of treatment. The primary endpoint for the treatment initiation phase was the mean change from baseline in serum potassium levels at week 4 or at the time of the first patiromer dose titration, if earlier.

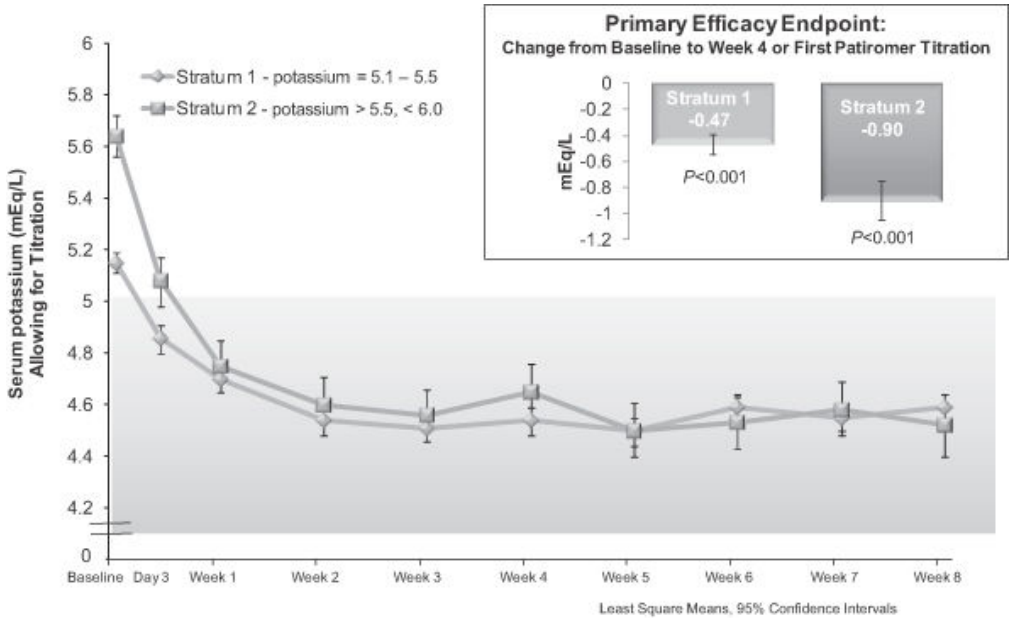
FIGURE 12: PHASE 2B STUDY DESIGN



Sources: Company reports and Wedbush Pacgrow Life Sciences

Treatment Initiation Phase: One of the primary goals of the trial was to determine a safe and efficacious starting dose for Phase 3. A dose finding interim data analysis was performed when about 120 patients had completed 8 weeks of treatment. Because there was no clear starting dose-dependent response to patiromer, the lowest effective dose tested was selected for the Phase 3 study. Based on the interim data, the selected starting doses were 8.4 grams/day and 16.8 grams/day for patients with baseline serum potassium levels of 5.1 to 5.5 mEq/L and above 5.5 mEq/L, respectively. A second interim analysis was conducted after all 306 patients had completed the 8-week treatment initiation phase and the primary endpoint was achieved with statistical significance. The mean change in serum potassium from baseline to week 4 or first patiromer titration was a reduction of 0.47 mEq/L ($p < 0.001$) and 0.90 mEq/L ($p < 0.001$) in Stratum 1 and Stratum 2, respectively. The mean serum potassium levels for patients in both strata decreased into the normal range within 1 week and remained stable for the remainder of the 8-week treatment period. Overall, safety results from the second interim analysis suggested that patiromer was well tolerated. About 30% of patients reported at least one AE, with the most common being GI symptoms (incidence ~1-10%). About 6% of patients reported an SAE, but all were assessed to be unrelated to patiromer. The incidence of hypokalemia was low, at about 2%.

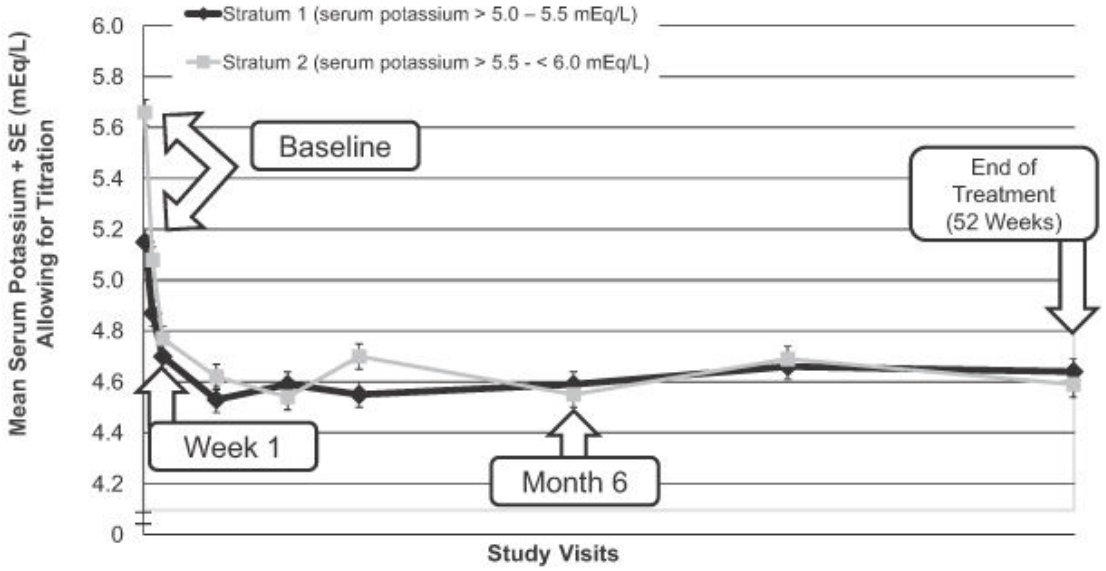
FIGURE 13: PHASE 2B TREAMENT INITIATION RESULTS



Sources: Company reports and Wedbush Pacgrow Life Sciences

Long-term Maintenance Phase Results: The mean serum potassium in both Stratum 1 and Stratum 2 remained in the target potassium range (3.8 to 5.0 mEq/L) throughout the 44-week maintenance phase. In addition, 85.5% (95% CI 78.7%, 90.8%) and 89.8% (95% CI 77.8%, 96.6%) of patients in Stratum 1 and Stratum 2, respectively, had serum potassium levels in the target range at week 52. Overall, patiromer was well tolerated when dosed twice daily for up to one year. SAEs occurred in 15% of patients, but all events were assessed to be unrelated to patiromer. The most common AEs were mild-to-moderate GI symptoms with constipation and diarrhea reported in 5-10% of patients. Importantly, the incidence of GI AEs did not increase over time with chronic dosing. Mild to moderate hypomagnesemia was reported in less than 10% of patients and there were no reports of severe hypomagnesemia.

FIGURE 14: PHASE 2B MAINTENANCE PHASE RESULTS



Sources: Company reports and Wedbush Pacgrow Life Sciences

PHASE 1 ONSET OF ACTION STUDY (RLY5016-301)

As part of the registration package, the company is conducting a Phase 1 open-label, single arm study with data anticipated in H1:14. The trial is designed to evaluate the time to onset of the potassium lowering action of patiromer in CKD patients with HK. About 15 patients will be enrolled and the study design includes a 48-hour treatment period followed by a 7-day post treatment visit for adverse events and serum potassium measurements. The change from baseline in serum potassium levels will be measured at 48 hours and at earlier time points to determine when the onset of potassium-lowering action occurs.

EARLY PATIROMER CLINICAL TRIALS

Summary. The clinical development of patiromer began with two Phase1 clinical trials in healthy volunteers. Along with a favorable safety profile, the key takeaways from those trials were that patiromer treatment resulted in a significant dose-dependent increase in fecal potassium excretion and a concomitant decrease in urinary potassium excretion across multiple dosing regimens. Following the successful Phase1 studies, the company conducted a Phase 2a proof-of-concept trial to assess the ability of patiromer to lower serum potassium levels in hemodialysis patients. The key findings included that patiromer was pharmacologically active and well tolerated in patients with impaired renal function. After the proof-of-concept trial, Relypsa conducted two Phase 2 studies to assess the ability of patiromer to prevent hyperkalemia in HF patients both with and without CKD who were on a RAASi. In the first prevention study (PEARL-HF), a fixed dose (30 grams per day) of patiromer was shown to reduce the incidence of hyperkalemia, while allowing a greater percentage of patients to increase their RAASi dose compared to placebo. However, 7% of patients experienced hypokalemia. As a result, the company initiated a second prevention trial (RLY5016-204) to evaluate a dose titration regimen of patiromer in an effort to lower the incidence of hypokalemia. With this new dose titration regimen, patiromer provided reliable control of serum potassium levels in about 91% of subjects.

PHASE 2 PREVENTION TRIALS

Phase 2 Prevention Trial (RLY5016-202 PEARL-HF): The purpose of PEARL-HF was to assess the safety and efficacy of patiromer in preventing hyperkalemia in normokalemic HF patients despite the use of higher doses of a RAAS inhibitor (spironolactone). Enrollment criteria included a requirement that subjects have a normal serum potassium level at baseline and that subjects had an

estimated GFR less than 60 mL/minute/1.73m^2, the onset of Stage 3 CKD, and/or had a history of hyperkalemia that led to discontinuation of a RAAS inhibitor or beta-blocker therapy. The trial evaluated a fixed daily dose of 30 grams of patiromer for four weeks versus placebo. Compared to placebo, patiromer significantly reduced mean serum potassium levels within 48 hours, prevented hyperkalemia and allowed a significantly greater percentage of HF patients to increase their dose of spironolactone. The statistically significant difference between groups in serum potassium level was sustained throughout the 4-week trial, despite the fact that patiromer-treated patients received a higher mean dose of spironolactone compared to placebo. Furthermore, 91% of patients treated with patiromer were able to increase their spironolactone dose versus 74% of placebo patients (p=0.019). In terms of safety, the AE rate was higher in patiromer-treated patients compared to placebo with the majority related to GI symptoms. AEs were generally mild or moderate, with one patient reporting severe flatulence. There were four SAEs, two in each arm, and all events were deemed unrelated to patiromer. In general, there were no clinically meaningful treatment-related changes in most laboratory parameters. Four patients (7%) experienced hypokalemia, but none resulted in any complications. There was also a small decrease in the average serum magnesium levels in the patiromer group, but no associated serious complications were reported.

Phase 2 Prevention Trial (RLY5016-204): The purpose of the second Phase 2 prevention trial was to determine whether initiating patiromer at a lower dose followed by a dose titration regimen would lower the incidence of hypokalemia while still preventing hyperkalemia in patients starting on a RAAS inhibitor (spironolactone). At the end of the 8 week treatment period, 91% of patients had serum potassium levels in the target range of 3.5 to 5.5 mEq/L and 84% of patients were in the range of 4.0 to 5.1 mEq/L. With the improved dose titration regimen, only 1 of 63 (1.6%) of patients developed hypokalemia. About 57% of patients reported at least one AE with GI symptoms being the most prevalent. AEs were generally mild to moderate. SAEs were reported in 10% of patients and were deemed unrelated to the trial.

RLY6002 for Type 2 Diabetes

Summary: RLY6002 is Relypsa's only other drug candidate that we are aware of. It is a preclinical candidate and was developed using the company's polymer drug discovery technology. The intended indication is as an adjunct to diet and exercise to improve glycemic control in adult Type 2 diabetics. Although Relypsa has a clinical development plan in place, it does not intend to further develop RLY6002 at this time as it devotes its resources to patiromer.

Analyst Biography

Ms. Moussatos is a Managing Director, Equity Research responsible for the coverage of stocks in the Emerging Pharmaceuticals sector. Liana joined Wedbush from Pacific Growth Equities where she was a Senior Research Analyst. Prior to that she came from UBS Global Asset Management where she was Director and Portfolio Manager of the UBS Global Biotech Funds for five years. Previously Liana was with Bristol-Meyers Squibb where she was a manager in University and Government Licensing External Science and Technology and she also worked with Sloan-Kettering Cancer Institute in the Office of Industrial Affairs and the National Cancer Institute in the Office of Technology Development.

Liana received a B.S. in Entomology and a M.S. in Zoology and Biochemistry from Clemson University and a Ph.D. in Plant Pathology from the University of California Davis and completed a postdoctoral research fellowship in Cellular and Molecular Physiology at the Yale School of Medicine.

Liana's Edge: Liana's industry and buy-side experience provide depth in her understanding of what investors need to know along with her 13 years experience in following healthcare stocks. Her pipeline valuation includes all drug candidates / disease indications in active development and provides investors with a stock value for each program.

Analyst Certification
I, Liana Moussatos, Ph.D., Richard Lau, CFA, 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/DisclosureQ313.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 September 30, 2013)	**Investment Banking Relationships (as of September 30, 2013)**
Outperform:55% Neutral: 41% Underperform: 4%	Outperform:14% 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.

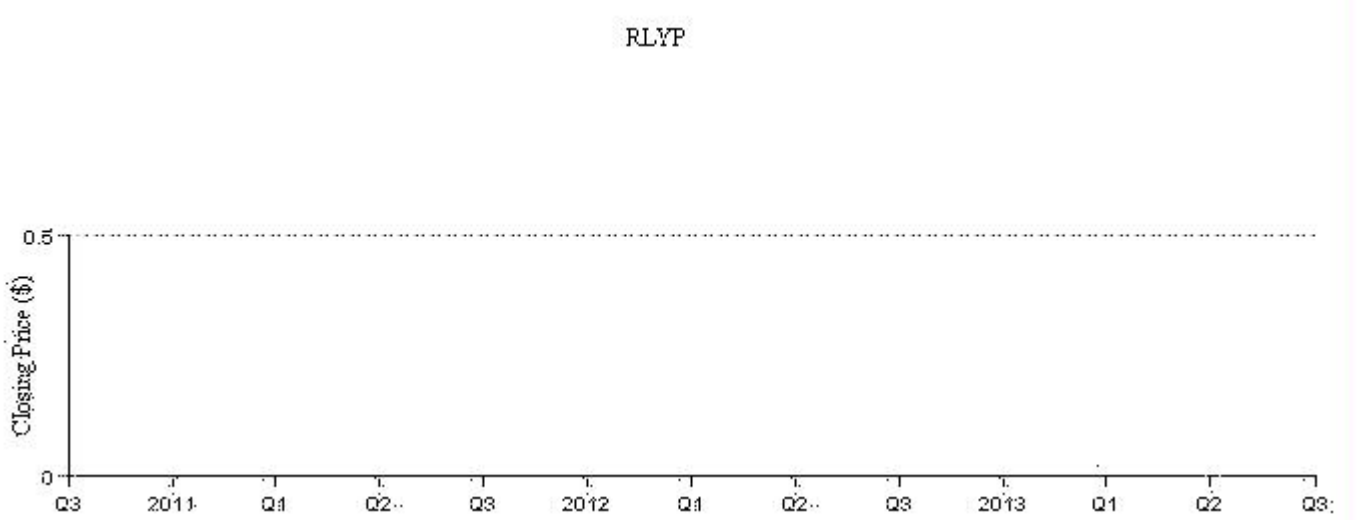
Wedbush Equity Research Disclosures as of December 9, 2013

Company	Disclosure
Relypsa	1,3,5,7

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.

OTHER DISCLOSURES

RESEARCH DEPT. * (213) 688-4505 * www.wedbush.com
EQUITY TRADING Los Angeles (213) 688-4470 / (800) 421-0178 * EQUITY SALES Los Angeles (800) 444-8076
CORPORATE HEADQUARTERS (213) 688-8000

WEDBUSH

EQUITY RESEARCH DEPARTMENT

(213) 688-4529

DIRECTOR OF RESEARCH
Mark D. Benson (213) 688-4435

MANAGER, RESEARCH OPERATIONS
Ellen Kang (213) 688-4529

RETAIL AND CONSUMER

Consumer Products
Rommel T. Dionisio (212) 938-9934
Kurt M. Frederick, CFA CPA (415) 274-6822

Footwear, Apparel and Accessories
Corinna Freedman (212) 668-9876
Alicia Reese (212) 938-9927

Healthy Lifestyles
Kurt M. Frederick, CFA CPA (415) 274-6822

Restaurants
Nick Setyan (213) 688-4519
Colin Radke (213) 688-6624

Specialty Retail: Hardlines
Joan L. Storms, CFA (213) 688-4537
John Garrett, CFA (213) 688-4523

Seth Basham, CFA (212) 938-9954

RETAIL/CONSUMER MARKET RESEARCH

Gabriella Santaniello (213) 688-4557

INDUSTRIAL GROWTH TECHNOLOGY

Clean Technology
Craig Irwin (212) 938-9926
Min Xu (212) 938-9925

Environmental Services / Building Products
Al Kaschalk (213) 688-4539
Taryn Kuida (213) 688-4505

Water and Renewable Energy Solutions
David Rose, CFA (213) 688-4319

TECHNOLOGY, INTERNET, MEDIA & SOCIAL MEDIA

Communications and Application Software / Internet
Shyam Patil, CFA (213) 688-8062

Communications Equipment
Rohit Chopra (212) 668-9871
Sanjit Singh (212) 938-9922
Ryan Flanagan (212) 938-9942

Computer Services: Financial Technology
Gil B. Luria (213) 688-4501
Aaron Turner (213) 688-4429

Enterprise Software
Steve Koenig (415) 274-6801
Kevin Ikeda (213) 688-4423

Entertainment: Retail
Michael Pachter (213) 688-4474
Nick McKay (213) 688-4343
Nick Citrin (213) 688-4495

Entertainment: Software
Michael Pachter (213) 688-4474
Nick McKay (213) 688-4343
Nick Citrin (213) 688-4495

Social Internet and E-Commerce
Michael Pachter (213) 688-4474
Nick McKay (213) 688-4343
Nick Citrin (213) 688-4495

Media
James Dix, CFA (213) 688-4315

Movies and Entertainment
Michael Pachter (213) 688-4474
Nick McKay (213) 688-4343
Nick Citrin (213) 688-4495

Semiconductors
Betsy Van Hees (415) 274-6869
Ryan Jue, CFA (415) 263-6669

LIFE SCIENCES

Biotechnology/Biopharmaceuticals/BioDefense
Gregory R. Wade, Ph.D. (415) 274-6863
David M. Nierengarten, Ph.D. (415) 274-6862
Christopher N. Marai, Ph.D. (415) 274-6861

Emerging Pharmaceuticals
Liana Moussatos, Ph.D. (415) 263-6626
Richard Lau, CFA (415) 274-6851

Healthcare Services - Managed Care
Sarah James (213) 688-4503

Medical Devices
Tao Levy (212) 938-9948

Medical Diagnostics and Life Sciences Tools
Zarak Khurshid (415) 274-6823

EQUITY SALES		EQUITY TRADING	
Los Angeles	(213) 688-4470 / (800) 444-8076	Los Angeles	(213) 688-4470 / (800) 421-0178
San Francisco	(415) 274-6800	San Francisco	(415) 274-6811
New York	(212) 938-9931	New York	(212) 344-2382
Boston	(617) 832-3700	Boston	(617) 832-3700

CORPORATE HEADQUARTERS
1000 Wilshire Blvd., Los Angeles, CA 90017-2465
Tel: (213) 688-8000 www.wedbush.com