

# **Proteon Therapeutics, Inc.** (PRTO)

Initiating Coverage at Market Outperform; The Demand for Elasticity

MARKET DATA	
Price	\$10.10
52-Week Range:	\$10.00 - \$12.00
Shares Out. (M):	12.9
Market Cap (\$M):	\$130.3
Average Daily Vol. (000):	52.0
Cash (M):	\$64
Cash/Share:	\$4.95
Enterprise Value (M):	\$250
Float (M):	14.7
LT Debt (M):	\$0
Short Interest:	0.0%
Source: Thomson Reuters and JMP Securities LLC	

FY DEC		2013A	2014E	2015E
Revenue (\$M)	1Q			\$0.0
	2Q		\$0.0A	\$0.0
	3Q		\$0.0	\$0.0
	4Q		\$0.0	\$0.0
	FY	\$0.0	\$0.0	\$0.0
EPS	1Q	(\$1.30)		(\$0.52)
	2Q	(\$0.33)	(\$1.30)A	(\$0.56)
	3Q	(\$0.28)	(\$0.33)	(\$0.59)
	4Q	(\$1.02)	(\$0.28)	(\$0.62)
	FY	(\$1.02)	(\$1.02)	(\$2.29)
Source: Company re	eports ar	nd JMP Securitie	s LLC	



MARKET OUTPERFORM | Price: \$10.10 | Target Price: \$22.00

# **INVESTMENT HIGHLIGHTS**

We are initiating coverage of Proteon Therapeutics with a Market Outperform rating and \$22 price target based on the synthesis of our discounted cash flow and compound annual growth valuation methodologies; ensuring that the fistula is here to stay. Proteon Therapeutics recently completed its IPO transaction on October 22 and is a development-stage drug company advancing PRT-201, a recombinant form of the enzyme elastase for use in maintaining vascular access in renal dialysis patients. Although Proteon is a single-product company, PRT-201 has already demonstrated compelling safety and efficacy in a highly informative, randomized Phase II trial that narrowly missed its primary endpoint of maintenance of vascular access in a population of dialysis patients. In our view, the Phase II trial significantly de-risked the planned Phase III study, as it not only will include those patient profiles with the best expected outcomes from the Phase II trial, but also utilizes the same clinical endpoints and most efficacious dose. We believe market demand for a proven therapy that can maintain vascular access will be robust, and we further believe that PRT-201 has the potential to become a \$1 billion product worldwide. We also note that Proteon holds full rights to the product.

Fistula first CMS/ESRD guidelines play to PRT-201's strengths. The home page of the End Stage Renal Disease Network Coordinating Center (http://esrdncc.org/) makes it clear that there is a significant push in the dialysis community to move toward the use of AV fistulae and away from tunneled dialysis catheters. Indeed, the program is quite specific in its nomenclature: "fistula first, catheter last." In our view, as the dialysis community moves more aggressively toward the use of fistulae for vascular access, the trend will provide a tailwind to the launch timing of PRT-201. We discuss this trend in further detail in this report.

#### Economics of the dialysis marketplace, PRT-201 in prime position for success.

The cost of managing vascular access dysfunction runs to nearly \$3 billion in the U.S. When a dialysis center loses a patient due to access failure, a lose-lose situation is created, meaning that revenue to the dialysis center is lost, and the system (mainly CMS) incurs higher procedure costs to restore vascular access. Patients are subject to an increased risk of infection while in the hospital or outpatient unit. In the Phase II trial, the median number of days' primary patency of radiocephalic AVFs was not reached in the 30mcg dose group (under study in the Phase III trial), strongly suggestive, in our view, of a clinically and economically meaningful benefit for PRT-201.

**Positive regulatory and commercial attributes for PRT-201**. PRT-201 has gained orphan drug designation and fast-track status from FDA, in our view, a testimony to the potential benefits the molecule has to offer. Further, reimbursement for PRT-201 will likely fall outside the CMS bundled dialysis payment system, and be reimbursed

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separately. In the early years of its launch, we believe the product will enjoy a markup for new technology (currently 6%) under the "ASP + 6" payment scheme. Finally, PRT-201 has patent protection to at least 2029.

Management team with the experience to successfully develop and commercialize PRT-201. PRTO is led by two veterans of the dialysis space - Tim Noyes, President and CEO, and Steven Burke, MD, SVP and CMO - with decades of experience from GelTex and Genzyme (Noyes was President of the Renal Division of Genzyme) and Dan Gottlieb, VP Strategic Marketing, has a background from Abbott (ABT, NC) Vascular. In our view, the PRTO management team has the requisite talent to design and execute not only a successful clinical and regulatory strategy, but also to place PRT-201 on the appropriate path for commercial success.

### **INVESTMENT THESIS**

Proteon Therapeutics is focused on the development of PRT-201 for the improvement of vascular access outcomes in patients undergoing radiocephalic surgery in preparation for hemodialysis. Current guidelines set forth by KDOQI, CMS, and the Fistula First Initiative state that arteriovenous fistulas (AVF) is the preferred method of vascular access, with significantly reduced infections and morbidity commonly associated with arteriovenous grafts or temporary catheter use. According to Proteon and JMP estimates, currently over 130,000 AVF surgeries are performed each year in the U.S., with over half of the procedures failing due to neointimal hyperplasia. There are no current therapies to improve AVF success rates, which, in our view, is supportive of a >\$1 billion market opportunity.

In preclinical models, and Phase I and II clinical trials in patients, Proteon has demonstrated that PRT-201, a recombinant human elastase, can reduce neointimal hyperplasia, provide up to a 63% reduction in the risk for loss of primary patency, and demonstrate a trend for improved secondary patency along with a dose dependent improvement in unassisted maturation. PRT-201 has received fast track designation and orphan drug status and method of use patents extending to 2024 and 2028, with the potential for extension to 2032.

Proteon plans to initiate two Phase III registration-directed trials, with the first to begin in 4Q14 and the second in 1H15, with final data expected in 2017. The company also plans to initiate EU directed Phase III trials after the read-out of the first U.S. Phase III trial and it will look for a partner to develop and commercialize the product in Japan.

Proteon plans to commercialize and market PRT-201 on its own in the U.S. by developing a concentrated specialty hospital sales force of 75-100 representatives targeting 1,300 hospitals, which account for nearly 90% of AVF placements in the U.S. PRTO also expects favorable reimbursement as vascular access procedures are normally done in the outpatient setting and are excluded from the ESRD bundle.

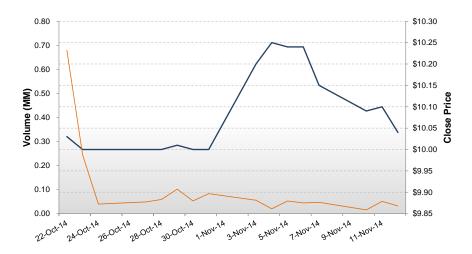
We believe that with the Phase II clinical efficacy demonstrated by PRT-201 in RCF surgery, the significant unmet clinical need in improving AVF surgeries, and by preventing vascular access failures and reducing the incidence of catheter use in the dialysis setting, Proteon will capitalize on a market-defining, first-in-class therapy.



# FIGURE 1. Upcoming Catalysts

Timing	Program	Catalyst
4Q14	PRT-201	Initiate First Phase III clinical trial in U.S.
1H15	PRT-201	Initiate second Phase III clinical trial in U.S.
Source: Company	y presentations	•

# FIGURE 2. PRTO Price Chart



Source: Thomson Reuters



### **VALUATION**

We derive our 12-month \$22 price target based on a synthesis of our discounted cash flow (DCF) and CAGR analyses. Each approach is built upon our forecast of sales of PRT-201 as used in radiocephalic AVF procedures. We exclude revenues from the use of PRT-201 in the brachiocephalic AVF, AVG, and peripheral arterial disease settings, as we await the initiation of registration-directed trials or additional supporting earlier stage clinical evidence.

FIGURE 3. Price Target Derivation

Synthesis of Valuation App	proacl	nes
Approach	Val	uation
DCF Analysis	\$	22.22
CAGR		22.29
Price Target	\$	22.00

Source: JMP Securities LLC

## Discounted cash flow methodology

We have constructed a discounted cash flow (DCF) model (Figure 4) utilizing contributions of revenue streams derived from the sales of PRT-201 in the U.S. and EU, with PRTO responsible for all sales and commercialization in this territory. Additionally, we assume the company will partner the development and commercialization of PRT-201 in Japan, resulting in a straight 15% royalty rate on all sales. We assume approval in the U.S. in 2018 after completion of two Phase III trials and approval in the EU in late 2019 after the completion of a Phase III trial. We project cash flows from these territories out to 2025. We apply a 15% terminal growth value given the patent's potential expiry in 2032.

We apply an initial tax rate of 0% that reaches 35% as the company attains profitability. We project peak revenues of \$1.256B in 2025. This equates to \$22.22 on a per share basis.

FIGURE 4. Discounted Cash Flow Model, 2014-2025E

Proteon (PRTO)														
Discounted Cash Flow Model			2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025
PRT-201 US Sales			-	-	-	-	91.2	141.6	127.0	202.2	376.7	498.1	560.4	580.0
PRT-201 EU Sales				-	-	-	-	89.2	133.2	192.8	259.8	445.6	593.3	658.4
PRT-201JPN Royalties			-	-	-	-	-	-	3.4	4.1	6.1	8.1	14.3	18.1
Total Revenues			-	-	-	-	91.2	230.8	263.5	399.1	642.6	951.8	1,168.0	1,256.4
R&D expenses			6.6	22.3	43.5	87.0	120.0	144.0	158.4	177.4	195.2	214.7	234.0	252.7
R&D as % of revenues								62.4%	60.1%	44.5%	30.4%	22.6%	20.0%	20.1%
SG&A expenses			4.8	7.2	11.6	15.6	21.1	34.8	38.3	49.7	67.2	90.7	108.8	125.1
SG&A as % of sales								15.1%	14.5%	12.5%	10.5%	9.5%	9.3%	10.0%
Operating Income (EBIT)			(11.4)	(29.5)	(55.1)	(102.6)	(60.8)	35.0	51.6	149.7	342.6	596.6	769.1	820.6
% Margin								24.7%	40.6%	74.0%	91.0%	119.8%	137.3%	141.5%
Taxes					-	-	-	5.2	12.9	52.4	119.9	208.8	269.2	287.2
Tax Rate			0.0%	0.0%	0.0%	0.0%	0.0%	15.0%	25.0%	35.0%	35.0%	35.0%	35.0%	35.0%
After-Tax Operating Income			(11.4)	(29.5)	(55.1)	(102.6)	(60.8)	29.7	38.7	97.3	222.7	387.8	499.9	533.4
Discounting Year			0.3	1.0	2.0	3.0	4.0	5.0	6.0	7.0	8.0	9.0	10.0	11.0
Discount Factor			1.07	1.30	1.69	2.20	2.86	3.71	4.83	6.27	8.16	10.60	13.79	17.92
PV			(10.6)	(22.7)	(32.6)	(46.7)	(21.3)	8.0	8.0	15.5	27.3	36.6	36.3	29.8
Terminal Value												Termin	al Value	198.4
Residual Value of CF	\$	226												
+ Cash and Cash Equivalents	\$	60												
Value of Company	\$	286												
- LT Debt														
Value of Equity	\$	286												
Price/share=	\$ 2	22.22												
		_												

Source: JMP Securities LLC



# **CAGR** methodology

We value PRTO shares at \$22.29 on a per share basis using a compound annual growth methodology. We begin by calculating the profitable PEG ratio (0.92), based on the mean 2015 P/E (16.9x) and a mean forward GAGR of 19.1% based on the three-year EPS for 2014-2016. Utilizing the projected EPS for PRTO in 2019 and a discount rate of 30%, we arrive at a valuation of \$22.29. Our assumptions and sensitivity analysis are detailed in Figures 5 and 6.

FIGURE 5. CAGR Valuation

Standardized CAGR Valuation	
Comparables	
Biotech Group P/E (2015)	16.9x
Biotech Group Forward CAGR ('14- '16)	19.1%
Valued Company	
Year used for discounting	2019
Price Target Year	2015
3-year EPS CAGR	75.1%
EPS in the discounting year	\$ 0.96
Discount Rate	30.0%
# Years for Discounting	4
Target Price	\$ 22.29

Source: JMP Securities LLC

FIGURE 6. Sensitivity Analysis

Sensitiv	vity	Analys														
		Discount Rate														
CAGR	2	27.0%	2	28.5%	3	0.0%	63	1.5%	3	3.0%						
69.1%	\$	22.52	\$	21.49	\$	20.51	\$	19.59	\$	18.72						
71.1%	\$	23.17	\$	22.11	\$	21.10	\$	20.16	\$	19.26						
73.1%	\$	23.82	\$	22.73	\$	21.70	\$	20.73	\$	19.81						
75.1%	\$	24.47	\$	23.35	\$	22.29	\$	21.29	\$	20.35						
77.1%	\$	25.13	\$	23.97	\$	22.89	\$	21.86	\$	20.89						
79.1%	\$	25.78	\$	24.60	\$	23.48	\$	22.43	\$	21.43						
81.1%	\$	26.43	\$	25.22	\$	24.07	\$	22.99	\$	21.97						

Source: JMP Securities LLC



### **COMPANY DESCRIPTION**

Proteon is a late-stage biopharmaceutical company engaged in the development of novel therapeutics to treat patients with vascular and renal disease. The company is developing a novel therapy to improve the outcomes of vascular access surgeries for dialysis patients. The company's lead product, PRT-201, is a recombinant human elastase solution applied to the exposed blood vessel during a surgical procedure to prevent remodeling of the blood vessel that can reduce vascular diameter and blood flow, resulting in high failure rates and fallback to ineffective and high-risk access methods, such as catheters. PRT-201 has completed Phase II clinical development, and demonstrated clinical efficacy in a subset of vascular access procedures known as radiocephalic arteriovenous fistulas (AVF). We estimate greater than 137,000 AVF procedures will be performed in the U.S. in 2014. The company plans to initiate the first of two Phase III trials by the end of 2014, and a second Phase III trial by 1H2015.

### **INVESTMENT RISKS**

**Clinical and regulatory.** If PRT-201 were to fail to show adequate efficacy in its Phase III trials, the FDA may not provide marketing approval in the U.S. If PRT-201 were to demonstrate unexpected serious adverse effects, this would also prevent market approval or potentially limit the scope of the intended market. Additionally, if the FDA and EMEA do not approve PRT-201, Proteon's stock price would likely suffer.

**Partnering**. Proteon plans to commercialize PRT-201. If it becomes necessary for it to develop and market any of its programs due to the inability to garner a partner, it may be difficult to develop an internal commercial structure. Management has limited experience in commercialization and marketing activities. In early 2014, Novartis declined its option to buy PRTO for \$550MM.

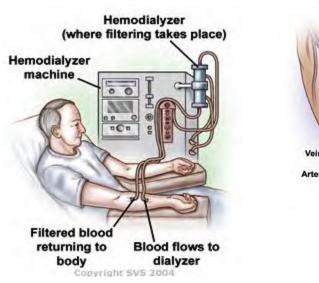
**Financial**. PRTO currently derives revenue capital raised through financing. The company sold ~6,110,000 shares in October 2014, raising gross proceeds of ~\$61.1MM. As a result, it is projected to finish 4Q14 with ~\$60.3MM in cash, equivalents, and marketable securities. We expect this funding to be able to carry the company to 2017. Like most non-profitable biotechnology companies, PRTO will likely need to seek additional financing, exposing current investors to dilutive risk.



### **CLINICAL OVERVIEW**

Dialysis is the most common method to treat kidney failure, with a U.S. prevalence of over 440,000 patients on dialysis per year. The hemodialysis procedure involves the continuous removal of blood from a patient, followed by filtration of the blood to remove metabolic byproducts, and then the return of the blood to the patient. This process is accomplished by accessing a patient's blood supply through a vascular access port, including an arteriovenous fistula, an arteriovenous graft, a catheter, or in some cases via peritoneal dialysis (Figure 7).

FIGURE 7. Dialysis and Vascular Access



Blood from dialyzer

Vein

Artery

Copyright.

SVS 2004

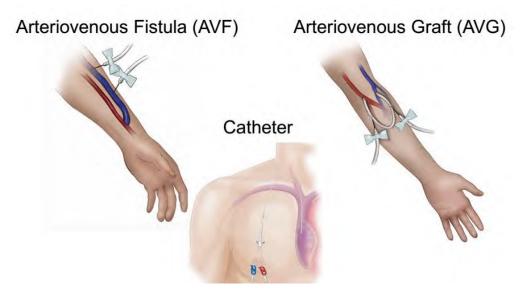
Source: Society for Vascular Surgery

The financial burden of dialysis to Medicare per year has been estimated to be nearly \$23 billion, or nearly \$88,000 per patient. The dialysis procedure is also a significant burden to the patient, with procedures lasting up to four hours per dialysis session, up to three times per week. Patients present with a number of comorbidities and in a significant percentage of cases, have never seen a nephrologist prior to beginning dialysis. Diabetes, vascular calcification, hypertension, and gastrointestinal dysfunction contribute to the high disease burden in these patients and in many cases, may be the fundamental cause of chronic kidney disease and eventual end-stage renal disease.

Adding to the disease and dialysis treatment burden is the therapeutic burden that patients will bear. Patients are required to take up to 19 pills per day to treat various sequellae including, but not limited to hyperphosphatemia, hyperkalemia, secondary hyperthyroidism, glucose control, hypercholesterolemia and high blood pressure medication. With up to 46% of the ESRD population presenting with diabetes, patients may also require daily insulin injections, resulting from the high percentage of diabetic patients who undergo dialysis. Finally, with such significant disease and treatment burden come frequent hospital visits, up to 12 hospital days/year. The United State Renal Data System reports that even with such high level of interventions, only 51% of ESRD patients remain alive three years after the start of ESRD therapy. Compared to patients for whom dialysis is not necessary, the rate of mortality is double for those receiving hemodialysis.



FIGURE 8. Forms of Vascular Access



Source: Society for Vascular Surgery

Studies have shown that the majority of hospitalization in patients receiving hemodialysis occurred due to cardiovascular conditions (19.1%), followed by access-related reasons and infections (11.5% each). The leading cause of death was cardiovascular in up to 51% of patients, followed by unknown/sudden causes (27.5%). Other causes of death include fluid overload, gastrointestinal hemorrhage, septicemia, liver disease, and pulmonary embolism.

Studies have shown that the form of vascular access can have a significant effect of patient mortality and downstream financial healthcare savings. As previously mentioned, vascular access is gained by several different methods, as illustrated in Figure 8.

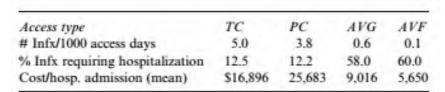
A retrospective analysis presented at the Society for Vascular Surgery in June 2014 by the Johns Hopkins Medical Center for the hemodialysis access distribution in the U.S. prevalent patient population shows a significant proportion of patients presenting with catheter access. Out of 502,380 patients studied, 418,932 patients (82.5%) were dialyzed via catheter, 71,316 patients presented with an AVF, and 17,543 patients (3.4%) were AVG. Overall survival estimates were assessed from the time of enrollment and hazard ratios calculated from this assessment. A patient dialyzed via an AVF had a 21% improved survival probability compared to catheter, followed by 18% when using an AVG. Additionally, studies from the University of Pittsburgh Medical Center have demonstrated that the infection rate is 50-fold higher with catheter dialysis access as illustrated in Figure 9. The costs of hospitalization due to catheter infection were dramatically higher, \$16,896 versus \$5,650.

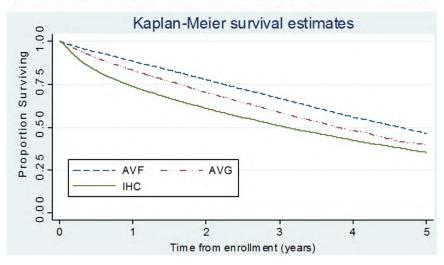
In light of the considerably increased mortality rates, infection rates, and costs associated with catheter dialysis, coupled with the striking number of catheter-based procedures to initiate dialysis, the ESRD Network and CMS have set forth guidelines and goals to increase the usage of AVF in the prevalent hemodialysis population. A National Vascular Access Improvement Initiative was established in 2003 called the Fistula First Initiative, (later changed to Fistula First



Catheter Last to further stress the need for change) with the goals of reaching or exceeding KDOQI guidelines of AVF incidence and prevalence rates of 50% and 40%, respectively, with the hope of reaching 65% AVF prevalence. Current prevalence levels have nearly reached these goals, with about 61% of the U.S. dialysis population accessing via AVF. On the other hand, incidence rates have not reached their goals, with only 20% of new patients beginning dialysis with an AVF.

FIGURE 9. Rates and Costs of Infections Due to Form of Dialysis and General Mortality Kaplan-Meir Analysis





Source: University of Pittsburgh, Johns Hopkins

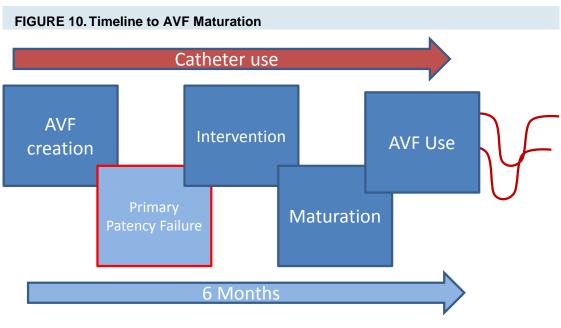
It is clear that the benefits of AVF come from decreased mortality and a significant impact on the cost of care. An AVF is also a longer lasting vascular access in healthy patients that can decrease the costs associated with generating vascular access. One of the major challenges in the Fistula First campaign has been in achieving a greater number of functioning fistulas. AVF access has been promoted as the "gold standard" because of its superior patency (unobstructed flow), low level of complications, and lower overall costs. The immense push to adopt AVF as the primary access method has dramatically shifted the prevalence of this form of access, but has also resulted in a dramatic alteration in the successful function of the fistulas.

According to numerous published reports from 1977 to 1985, acceptable fistula failure rates were approximately 10%, with one-year primary patency of 70-80%. Current reports from the past decade indicate a primary failure rate between 30-70%, with one-year primary patency rates of 40-70%. Failures generally arise from early thrombosis and failure of the fistulas to mature.



The increases in failure to mature rates have partially contributed to the higher use of catheters, as the patient must begin dialysis while various interventions are performed to create permanent access. Compared to rates of incident temporary catheter use in 1990 of about 9%, current temporary incident catheter use has ballooned to well over 60%. Risk factors that promote AVF failure, including a high degree of arteriosclerosis, vascular calcification, and other peripheral vascular disease are also risk factors for increased use of catheter-based access.

The greatest rate of catheter use occurs during the fistula maturation period. Studies have demonstrated that the sequence of events leading to temporary catheter use stems from the fistula maturation schedule detailed in Figure 10.



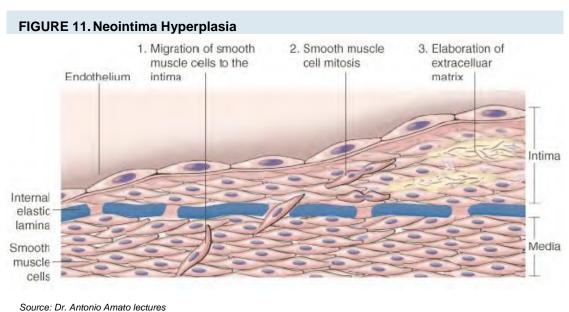
Source: JMP Securities with information from Lok, 2007

Research has actively pursued the reduction of primary patency failure as a means to reduce the time required for patients to be dialysed via temporary catheter. Equally important to the Fistula First guidelines has been the pressure to progressively bring temporary catheter dialysis below 10% in order to reduce the accompanying health and financial risks associated with catheter dialysis. In 2007, the average cost of AVF creation and management was \$11,609/year. Concomitant catheter insertion and management is ~\$13,000. If primary patency loss occurs, the costs nearly double, with recent estimates in 2012 from Mt. Sinai Medical Center estimating the costs of maintaining AVF at one year at up to \$23,942, and after two years at up to \$53,251, with much of the cost likely occurring due to primary patency failure and long-term catheter use leading to infection, hospitalization, and various interventions to restore patency.



## Elastase as a means to improve primary patency

As highlighted above, the AVF vascular access method is ideal to generate the blood flow required for dialysis (~400ml/min). This method provides better longevity and fewer interventions, but requires significant time to maturation and is also prone to failure with >50% of AVFs resulting in a failure to mature. Furthermore, after interventions to restore primary patency, ~25% of AVFs will result in the loss of secondary patency and will typically result in abandonment of the AVF and a second intervention to generate a new permanent access. Failures arise primarily due to neointimal hyperplasia - an inflammatory and wound healing response that occurs after surgical intervention.



Source: Dr. Antonio Amato lectures

The process of neointimal hyperplasia begins with damage to the arterial wall, followed by significant recruitment of platelets and inflammatory cells, with the further release of cytokines and extracellular matrix proteins. These growth factors stimulate the proliferation of vascular smooth muscle cells that migrate to the site of the injury, increasing intimal thickness through extracellular matrix deposition, and eventual stenosis and vessel occlusion.

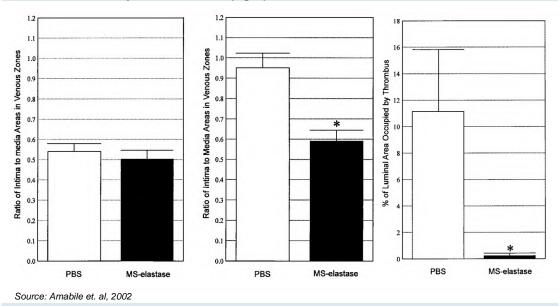
It has been hypothesized that disruption of the extracellular matrix, specifically the elastin fiber integrity, can result in two outcomes that may prevent neointimal hyperplasia: 1) selective disruption of the elastin matrix can prevent smooth muscle cell migration by preventing chemotaxis along this substrate; and 2) chemotactic gradient formation disruption.

The importance of elastin in smooth muscle cell migration has been documented, including studies of elastin knockout mice, examinations of human atherosclerotic plaque specimens, pig models of transplant arteriopathy, and rodent balloon-injury models of restenosis.

In order to study the potential of elastin disruption and its effect on vascular neointimal formation, preclinical studies done by *Amabile et.al*, explored the use of elastase to disrupt elastin in the perivascular region of a rabbit model of an artery graft. Neointimal hyperplasia was measured as the ratio of intima to media areas in venous zones after elastase application in vein grafts. A significant decrease was observed in treatment versus control PBS (Figure 12).



FIGURE 12. Rabbit Vein Graft Neointimal Formation 7 days (left) or 28 Days (center) and Thrombolytic Formations (right) After Treatment



Additionally, examination of thrombus formation, one of the major complications giving rise to the loss of primary patency and AVF abandonment, showed dramatic effects. Measurements were taken of the luminal area occupied by the thrombus seven days after the procedure and elastase treatment with PBS control demonstrating ~11% occupancy, and elastase treatment reflecting almost none (Figure 12).

#### Phase I clinical trial

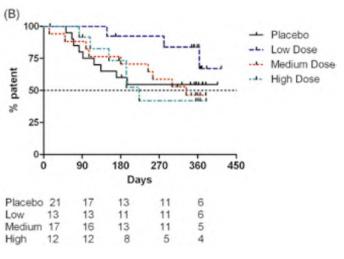
In light of the successful utilization of elastase in animal studies, Proteon initiated Phase I/II safety trials in a sequentially adaptive, randomized, double-blind, placebo-controlled, dose escalation study of a single application of PRT-201 in 66 patients undergoing AVF surgery for hemodialysis, separated into 11 cohorts of 9 doses: low dose (0.0033, 0.01, 0.033 mg), medium dose (0.1, 0.33, 1.0 mg), and high dose (3.0, 6.0, 9.0 mg). The small study group prevented powering to achieve statistically significant efficacy.

There were no statistically significant differences in the proportion of placebo and PRT-201 treatment-related adverse events, with the majority of reports consistent with medical conditions experienced by chronic kidney disease patients undergoing AVF surgery. One patient experienced a thrombotic embolism that had presented in a previous and subsequent AVF procedure and was deemed to be due to heparin-induced thrombocytopenia, unrelated to PRT-201. Only one out of the 66 patients tested positive for anti-PRT-201 antibodies following treatment in the 6 mg cohort. No skin-related adverse events were identified in this patient, suggesting a low level of antigenicity.

There was no statistically significant difference between groups in determining the primary outcome of ≥25% increase in the diameter of the AVF, nor in the secondary endpoints of increase of ≥25% in AVF outflow. An exploratory analysis demonstrated significant decreased risk of unassisted primary patency loss in the low-dose treatment cohort (Figure 13).



FIGURE 13. Kaplan Meir Plots of Unassisted Primary Patency, Excluding Three Early Surgical Failures



Source: Peden et. al, 2013

This study demonstrated PRT-201 to be well tolerated and safe, with no significant treatment-related adverse events in the population of patients undergoing vascular access surgery. Additionally, this population presents with a number of significant comorbidities and the use of PRT-201 did not exacerbate any of these conditions. Encouragingly, in this small population, a significant effect was seen in a post-hoc cohort analysis that supported the advancement of PRT-201 into Phase II clinical trials.



#### Phase II trial

This Phase II study randomized 169 patients, with 151 receiving treatment; the study design is illustrated in Figure 14. Based on Phase I clinical efficacy seen in the low dose cohort, doses in this Phase II trial included 59 patients who received PRT-201 at 10 ug, with 51 eligible for analysis, and 53 patients receiving 30 ug, with 49 being eligible for analysis, while 57 patients receiving placebo of which 51 were eligible for analysis. Eighteen patients did not receive intervention due to the withdrawal of consent, a change in procedure, or ineligibility at trial initiation.

# FIGURE 14. Clinical Trial Design

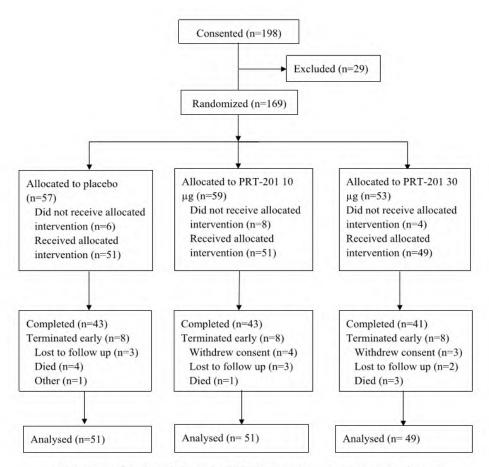


Fig 1. Patient flow through the study. PRT-201, Recombinant type I pancreatic elastase.

Source: Hye et.al, 2014

No significant patient baseline characteristics were noted, except for a higher baseline BMI in the 30 ug group. As PRT-201 is locally acting, patient BMI is not necessarily an important factor. Also, as would be expected, the patient population covers a wide spectrum of comorbidities, including a significant proportion of patients presenting with diabetes (39-55%), and cardiovascular disease (18-22%) (Figure 15).



FIGURE 15. Patient Baseline Characteristics

		PRT	T-201
Variable	$\begin{array}{c} Placebo\\ (n=51) \end{array}$	$10  \mu g$ $(n = 51)$	$30 \mu g$ $(n = 49)$
Male, %	63	55	55
White, %	63	78	74
Age, mean ± SD, years	$59 \pm 15$	$59 \pm 18$	$59 \pm 15$
≥65 years, %	35	45	31
BMI, mean ± SD, kg/m <sup>2</sup>	$31 \pm 8$	$31 \pm 8$	$35 \pm 8$
RCF, %	47	45	41
IHD, %	49	59	57
PAD, %	29	20	22
CVD, %	18	22	22
Predialysis, %	57	55	71
CKD due to DM, %	39	43	55
CKD due to HTN, %	35	28	22
Duration CKD, mean ± SD, months	$44\pm44$	$54 \pm 66$	$60 \pm 75$
Tobacco free, %	55	49	41
Local anesthesia, %	53	57	43
Nerve block, %	26	26	35
Fluid dilation, %	80	69	76
Mechanical dilation, %	37	35	31
Running sutures, %	94	94	96
Non-absorbable sutures, %	92	92	96
Exposed vein length, mean ± SD, cm	$3.4 \pm 1.0$	$3.5 \pm .8$	$3.5 \pm 1.0$
Arteriotomy length mean ± SD, cm	$0.9 \pm 0.3$	$0.9 \pm 0.3$	$0.8 \pm 0.3$

BMI, Body mass index; CKD, chronic kidney disease; CVD, cerebrovascular disease; DM, diabetes mellitus; HTN, hypertension; IHD, ischemic heart disease; PAD, peripheral artery disease; PRT-201, recombinant type I pancreatic elastase; RCF, radiocephalic fistula; SD, standard deviation.  $^{3}P < .05$ .

**Profile** 

FIGURE 16. Safety and Adverse Event

		PRT	-201
Event	Placebo (n = 51), No. (%)	10 μg (n = 51), No. (%)	30 μg (n = 49) No. (%)
Any adverse event	42 (82)	39 (77)	43 (88)
AVF thrombosis	13 (26)	8 (16)	7 (14)
Steal syndrome	7 (14)	2(4)	6(12)
Hypoesthesia	7 (14)	6 (12)	6(12)
AVF incision pain	5 (10)	9 (18)	9 (18)
AVF site complication	5 (10)	4(8)	4(8)
Peripheral edema	5 (10)	0 (0)	2(4)
Nausea	5 (10)	1(2)	2(4)
Arterial stenosis	4(8)	5 (10)	0(0)
Paresthesia	1(2)	1(2)	5 (10)
Erythema	1(2)	1(2)	5 (10)

AVF, Arteriovenous fistula; PRT-201, recombinant type I pancreatic elastase.  $^{a}$ Treatment of emergency adverse events occurring in at least 5% of placebo or the combined PRT-201 treatment groups.

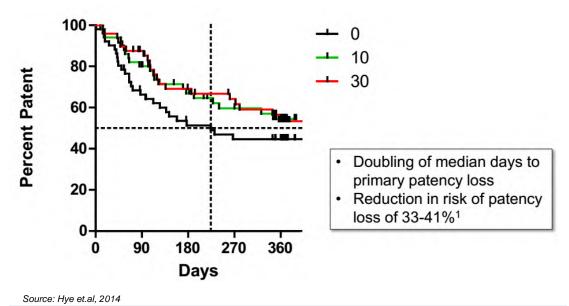
Source: Hye et.al, 2014 Source: Hye et.al, 2014

As shown in Figure 16, the rate of any adverse event was similar across all patient cohorts (77-88%), albeit high among all patient cohorts, indicative of the general poor health of patients being admitted to dialysis. There were no significant differences between PRT-201 treatment groups or placebo. Pre-treatment PRT-201 antibodies were detected in four patients; post-treatment antibodies were detected in one placebo patient with the highest detection titers of 1:2, a relatively low signal. Retests at six months were all negative.

Primary patency was initially measured for all patients receiving AVF access, which demonstrated a doubling of the median days for the loss of primary patency. The median primary patency time for placebo was 223 days and ≥365 days in the PRT-201 groups. The risk of primary patency loss was not numerically greater in the treatment cohorts, but not statistically significant across all patient cohorts - 10 ug (Hazard Ratio (HR) 0.69; 95% confidence interval [CI], 0.39-1.22; p= 0.19) or 30 ug (HR, 0.67; 95% CI, 0.38-1.19; p=0.17).

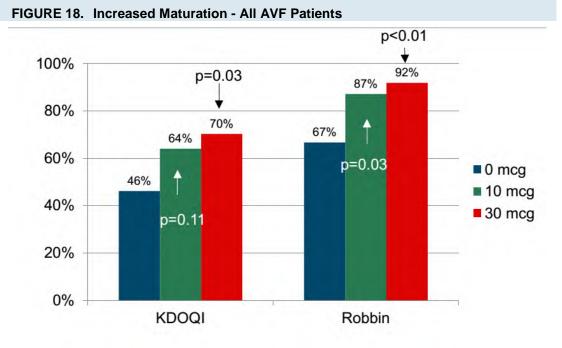






The percentages of patients with unassisted maturation at three months was statistically significant, according to both Robbin (92%) and KDOQI (70%) criteria at the 30 ug dose, with a dose-dependent improvement among the cohorts (Figure 18).

se-dependent improvement among the cohorts (Figure 18).

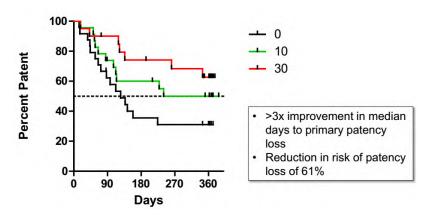


Source: Hye et.al, 2014



Cox proportional hazard modeling of patients with radiocephalic AVF placement demonstrated a dose dependent and statistically significant increase in the primary patency in patients with a RCF. Median patency was 125 days in the placebo group and >365 days in the PRT-201 groups. At one year, 31%, 50%, and 63% of placebo, 10-mg, and 30-mg patients retained primary patency. The risk of primary patency loss was not significantly reduced in the 10 ug cohort (HR, 0.59; 95% CI, 0.28-1.28; p= 0.18) and significantly reduced by 30 ug (HR, 0.37; 95% CI, 0.15-.91; p=0.02) vs. placebo.

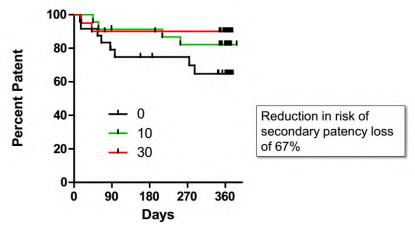




Source: Hye et. al, 2014

Secondary patency was retained in the subset of patients with RCF at 65%, 82%, and 90% of placebo, 10-ug, and 30 ug treatment cohorts at one year. The risk of SP loss, although numerically lower, was not significantly different versus placebo for the 10 ug treatment (HR, 0.45; 95% CI, 0.14-1.51; p=0.19) or 30 mg (HR, 0.27; 95% CI, 0.06-1.29; p= 0.08) (Figure 20).

FIGURE 20. Secondary Radiocephalic AVF Patency



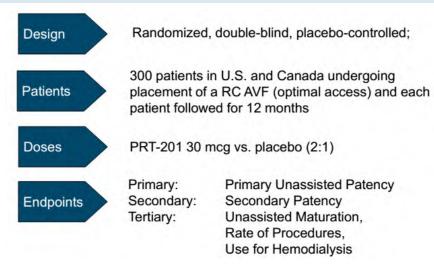
Source: Hye et. al, 2014



#### Planned Phase III

In the subgroup of patients who received a RCF, 30ug was associated with a 63% reduction in the HR for loss of primary patency and a trend for improved secondary patency, along with a dose-dependent improvement in unassisted maturation. With these compelling Phase II results in RCF in hand, Proteon is advancing PRT-201 into Phase III trials for this treatment population. As previously outlined, there is significant unmet clinical need for treatments to improve AVF success rates and decrease the incidence of catheter utilizations in hemodialysis. Additionally, the KDOQI guidelines favor placement of RCF's in patients because of the preservation of significant access points along the arm for further vascular surgeries, peripheral arterial disease and stenosis will frequently cause abandonment of existing fistulas.

#### FIGURE 21. First Phase III Trial



Source: Company Reports

Proteon is planning two well-controlled Phase III trials, each with 300 subjects undergoing RCF surgery with >95% power for the primary endpoint of two-fold improvement of primary unassisted patency. If the Phase II results are reflective of a possible outcome, then the three-fold improvement in primary unassisted patency will result in 98% power and overwhelming significance (Figures 21 & 22).

The second planned Phase III trial will be powered to see a 15% increase in secondary patency among ~300 patients undergoing vascular access surgery and receiving an RCF. Again, if Phase II results are replicated in this 30 ug treatment arm, resulting in ~25% increase in secondary patency, the results will be 99% powered, supportive of significant results.



#### FIGURE 22. Second Phase III Trial

Patients

Patients

Randomized, double-blind, placebo-controlled;

~300 patients in U.S. and Canada undergoing placement of a RC AVF (optimal access) and each patient followed for 12 months

PRT-201 30 mcg vs. placebo (2:1)

Endpoints

Primary: Primary Unassisted Patency
Secondary: Secondary Patency
Tertiary: Unassisted Maturation,

Unassisted Maturation, Rate of Procedures, Use for Hemodialysis

Source: Company Reports

### **COMMERCIAL POTENTIAL**

In Figure 23, we detail our assumptions for the vascular access market and arrive at our addressable patient population through a combination of prevalence and incidence modeling. We assume a dialysis prevalence population of 441,533, based on USRDS collected data. We calculate an expected conversion rate from any form of access (primarily catheter) to AVF of 38%, based on a retrospective analysis done by *Bradbury et.al, 2009*. Of this population, we further assume a conversion rate to AVF vascular access of 51%. We then assume conversions will be 50% brachiocephalic and 40% radiocephalic, roughly in line with our collected data. This provides us with an addressable RCF patient population for 2014 of 34,673 patients. We then collected reported incidence data on new dialysis starts according to U.S. FFCL collected data, which is estimated to be 27,661 new patients initiating dialysis with an AVF. Assuming a 64% success rate in AVF surgery, we estimate that 43,220 patients will undergo AVF surgery. Again, assuming a split of 50% BCF and 40% RCF, we arrive at an RCF incidence population of 20,177. Together this population encompasses ~54,820 addressable RCF patients. Assuming a cost per procedure of \$14,000, justifiable given the high price of vascular access failure, we estimate peak sales in the U.S. of \$580MM in 2025 (Figure 23).

# FIGURE 23. AVF Market Model

Dialysis Vascular Access Surgeries Model													
US Model	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E
Epidemiology													
Dialysis Conversions													
Dialysis Prevalence	441,533	447,273	456,218	465,343	474,649	484,142	493,825	503,702	513,776	524,051	534,532	545,223	556,127
% growth	2.0%	2.0%	2.0%	2.0%	2.0%	2.0%	2.0%	2.0%	2.0%	2.0%	2.0%	2.0%	2.0%
% conversion	38.0%	38.0%	38.0%	38.0%	38.0%	38.0%	38.0%	38.0%	38.0%	38.0%	38.0%	38.0%	38.0%
% conversion to AVF	51.0%	51.0%	51.0%	51.0%	51.0%	51.0%	51.0%	51.0%	51.0%	51.0%	51.0%	51.0%	51.0%
Total AVF conversions	85,569	86,681	88,415	90,183	91,987	93,827	95,703	97,617	99,570	101,561	103,592	105,664	107,777
% brachiocephalic	50.0%	50.0%	50.0%	50.0%	50.0%	50.0%	50.0%	50.0%	50.0%	50.0%	50.0%	50.0%	50.0%
% radiocephalic	40.0%	40.0%	40.0%	40.0%	40.0%	40.0%	40.0%	40.0%	40.0%	40.0%	40.0%	40.0%	40.0%
Addressable Radiocephalic Conversion Patients	34,228	34,673	35,366	36,073	36,795	37,531	38,281	39,047	39,828	40,624	41,437	42,266	43,111
New Starts-Dialysis Vascular Access Incidence	136,471	164,826	189,549	208,504	218,930	221,119	222,667	224,225	225,795	227,376	228,967	230,570	232,184
% growth Q/Q or Y/Y	24.7%	20.8%	15.0%	10.0%	5.0%	1.0%	0.7%	0.7%	0.7%	0.7%	0.7%	0.7%	0.7%
Vascular Access Surgeries													
AVF patients	27,661	32,283	37,910	41,701	43,786	44,224	44,533	44,845	45,159	45,475	45,793	46,114	46,437
% total	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%
% successful AVF surgeries	64%	64%	64%	64%	64%	64%	64%	64%	64%	64%	64%	64%	64%
Estimated total # AVF surgeries	43,220	50,443	59,234	65,158	68,416	69,100	69,583	70,070	70,561	71,055	71,552	72,053	72,557
% brachiocephalic	50.0%	50.0%	50.0%	50.0%	50.0%	50.0%	50.0%	50.0%	50.0%	50.0%	50.0%	50.0%	50.0%
% radiocephalic	40.0%	40.0%	40.0%	40.0%	40.0%	40.0%	40.0%	40.0%	40.0%	40.0%	40.0%	40.0%	40.0%
Addressable New Radiocephalic Patients	17,288	20,177	23,694	26,063	27,366	27,640	27,833	28,028	28,224	28,422	28,621	28,821	29,023
Total Addressable Radiocephalic Patients	51,516	54,850	59,060	62,136	64,161	65,171	66,115	67,075	68,052	69,046	70,058	71,087	72,134
PRT-201 Penetration (%)						10%	15%	13%	20%	36%	46%	50%	50%
# of procedures utilizing PRT-201						6,517	9,917	8,720	13,610	24,857	32,227	35,543	36,067
Sales Calculations	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E
Cost per procedure						14,000	14,280	14,566	14,857	15,154	15,457	15,766	16,082
% Price Increase						2.0%	2.0%	2.0%	2.0%	2.0%	2.0%	2.0%	2.0%
Gross Sales of PRT-201 - US (\$MM)			\$ -	\$ -	\$ -	\$ 91	\$ 142	\$ 127	\$ 202	\$ 377	\$ 498	\$ 560	\$ 580

Source: JMP Securities LLC, FistulaFirst, USRDS

# FIGURE 24. PRTO Revenue Model

Proteon (PRTO)																	
PRTO Revenue Build (\$MM)	2	2018E		2019E		2020E		2021E		2022E		2023E		2024E		2025E	
PRT-201- US	\$	91	\$	142	\$	127	\$	202	\$	377	\$	498	\$	560	\$	580	
PRT-201- EU		-		89		111		165		219		392		498		538	
PRT-201- JPN		-		-		22		28		41		54		95		120	
Total PRT-201 Sales WW	\$	91	\$	231	\$	260	\$	395	\$	636	\$	944	\$	1,154	\$	1,238	

Source: JMP Securities LLC, Company reports



#### **PATENTS**

Proteon owns 20 issued patents and has 26 pending patent applications. The patents roughly fall into two categories - those that protect production methods and formulations of elastase and patents covering therapeutic uses of elastase. The formulation family consists of one issued patent in the U.S., one in the EU, and additional worldwide patents. The expected expiration of these patents is 2028, with PTE extending expiry to 2029, exclusive of a possible NCE extension for an additional five-years of marketing exclusivity. The therapy family of patents includes seven in the U.S. and multiple worldwide patents set to expire in 2021, exclusive of PTE.

#### MANAGEMENT TEAM AND BOARD OF DIRECTORS

Timothy P. Noyes, President and Chief Executive Officer. Timothy Noyes joined Proteon in 2006 as President and Chief Executive Officer and has also been a member of the board of directors since joining the company. From 2002 to 2006, Mr. Noyes served as Chief Operating Officer of Trine Pharmaceuticals, Inc., a biopharmaceutical company. Before joining Trine, Mr. Noyes held several management positions with GelTex Pharmaceuticals from 1996 to 2001, prior to its acquisition by Genzyme Corporation. After the acquisition, from 2001 to 2002, he held the position of President, Renal Division and President, GelTex Pharmaceuticals. Prior to GelTex, he worked for several years at Merck & Co. across multiple roles in its hypertension and heart failure group and managed care division, and on its Vasotec and Prilosec products. Mr. Noyes received an A.B. from Harvard College and an M.B.A. from Harvard Business School.

**Steven K. Burke, M.D.,** Senior Vice President and Chief Medical Officer. Steven Burke, M.D., joined Proteon in 2006 as Senior Vice President and Chief Medical Officer. Prior to joining Proteon, Dr. Burke served as Senior Vice President of Medical and Regulatory Affairs and Vice President of Clinical Research at Genzyme Corporation, where he worked from 2000 to 2006. From 1994 to 2000, Dr. Burke held roles at GelTex Pharmaceuticals, including Vice President of Clinical Research and Medical Director, and before that he held positions at Glaxo. Dr. Burke received an A.B. from Harvard College and an M.D. from Cornell University Medical College. He completed a medical residency and fellowship at Brigham and Women's Hospital and is certified by the American Board of Internal Medicine.

George A. Eldridge, Senior Vice President and Chief Financial Officer. George Eldridge joined Proteon in 2013 as Chief Financial Officer. Prior to joining Proteon, from 2009 to 2013, Mr. Eldridge served as a consultant to companies in the biotechnology industry, acting as a chief financial officer and providing advisory services. From 2006 to 2009, Mr. Eldridge was Chief Financial Officer of Targanta Therapeutics Corporation until its acquisition by The Medicines Company. Before working at Targanta, Mr. Eldridge served as Chief Financial Officer of Therion Biologics from 2002 to 2006, and prior to that he served as Chief Financial Officer of Curis (previously Ontogeny) and Boston Life Sciences. Prior to working in the biotechnology field, Mr. Eldridge was an investment banker at Kidder Peabody & Co. He holds a B.A. from Dartmouth College and an M.B.A. from the University of Chicago.



**Daniel P. Gottlieb**, Vice President, Marketing and Business Development. Daniel Gottlieb joined Proteon in 2007 and has served as Vice President, Marketing and Business Development since 2013, prior to which he was the Senior Director of Marketing and Business Development from 2010 until 2013 and Director of Marketing and Business Development from 2007 until 2010. Prior to joining Proteon, Mr. Gottlieb served as Strategic Marketing Manager of Endovascular Products at Abbott Vascular from 2006 to 2007. Prior to that, Mr. Gottlieb spent seven years, from 1999 to 2006, at Guidant Corporation in a variety of roles, including marketing and market research, strategic planning, and business development and corporate venture investing as part of Guidant's Compass Group. Mr. Gottlieb holds a B.A. from the University of Pennsylvania and an M.B.A. from the Tuck School of Business at Dartmouth College.

Marco D. Wong, M.D., Ph.D. Medical Director. Marco Wong, M.D., Ph.D., joined Proteon in 2006 and has served as Medical Director since 2011, prior to which he was Associated Director of Research and Development from 2009 until 2011 and Physician Scientist/Senior Scientist from 2006 until 2009. Prior to joining Proteon, Dr. Wong served as a Post-doctoral Research Associate at the Stowers Institute for Medical Research from 2003 to 2006, where he conducted genetic and molecular analysis of stem cells and germ cell development. He holds a B.S. from California State University and an M.D. and Ph.D. from Wayne State University School of Medicine.

#### **Board of Directors**

Timothy P. Noyes President and Chief Executive Officer (See Management biography)

Hubert Birner, Ph.D. Managing Partner, TVM Capital. Hubert Birner, Ph.D., has served as a member of the board of directors since 2007. Dr. Birner is the managing partner of TVM Capital, a venture capital firm, which he joined in 2000. Before joining TVM Capital, Dr. Birner served as Head of Business Development Europe and Director of Marketing for Germany at Zeneca from 1998 to 2000. Dr. Birner joined Zeneca from McKinsey & Company's European Health Care and Pharmaceutical practice where he worked from 1995 to 1998. From 1992 to 1994, Dr. Birner was an Assistant Professor for biochemistry at the Ludwig-Maximilian-University in Munich. Dr. Birner currently serves as Chairman of the Board of Argos Therapeutics Inc. and Spepharm Holding BV and he previously served as a member of the board of directors of Horizon Pharma, Evotec AG, and BioXell SPA. Dr. Birner received an M.B.A. from Harvard Business School and a Ph.D. in biochemistry from Ludwig-Maximilian-University Munich, where he graduated summa cum laude.

Garen Bohlin Consultant, Life Sciences and Healthcare Companies. Garen Bohlin has served as a member of the board of directors since September 2014. Since May 2012, Mr. Bohlin has served as a consultant to various life sciences and healthcare companies. From January 2010 until April 2012, he served as Executive Vice President of Constellation Pharmaceuticals, a biopharmaceutical company. Prior to joining Constellation Pharmaceuticals, Mr. Bohlin served as Chief Operating Officer of Sirtris Pharmaceuticals, a biopharmaceutical company, from 2006 to December 2009. Mr. Bohlin was the founding Chief Executive Officer of Syntonix Pharmaceuticals, Inc., a biopharmaceutical company, from 1999 through December 2008. Earlier in his career, he held multiple executive positions at Genetics Institute, a biopharmaceutical company, and was a partner at Arthur Andersen & Co., a public accounting and consulting organization. Mr. Bohlin currently serves on the board of directors of Tetraphase Pharmaceuticals and Karyopharm Therapeutics, both NASDAQ listed, and Acusphere, Inc. He also served on the board of directors for Targanta Therapeutics from 2007 to 2009, SpringLeaf Therapeutics from 2010 to 2013 and Precision Dermatology from 2012 to July 2014. Mr. Bohlin received his B.S. in accounting and finance from The University of Illinois.



John G. Freund, M.D. Skyline Ventures. John G. Freund, M.D., became a member of the board of directors in 2014. Dr. Freund co-founded Skyline Ventures, a venture capital firm, in 1997, where he has served as a partner since its founding. Prior to joining Skyline, Dr. Freund served as managing director in the private equity group of Chancellor Capital Management from 1995 to 1997. In 1995, he co-founded Intuitive Surgical, Inc. and served on its board of directors until 2000. From 1988 to 1994, Dr. Freund served in various positions at Acuson Corporation, now part of Siemens, most recently as Executive Vice President. Prior to joining Acuson, Dr. Freund was a general partner of Morgan Stanley Venture Partners from 1987 to 1988. From 1982 to 1988, Dr. Freund worked at Morgan Stanley & Co., where he co-founded the Healthcare Group in the Corporate Finance Department. Dr. Freund currently serves as a member of the board of directors of the following public companies: XenoPort, Inc., Tetraphase Pharmaceuticals, Inc. and Concert Pharmaceuticals, Inc. He was on the board of MAKO Surgical Corp. from October 2008 until its acquisition in 2013. Dr. Freund also serves as a member of the board of directors of the following private companies: Advion, Inc., Collegium Pharmaceuticals, Inc., DiscoveRx Corporation, SI Bone, Inc. and Sutro Biopharma, Inc. He is a director of three mutual funds managed by Capital Research and Management. He is a member of the Advisory Board for the Harvard Business School Healthcare Initiative and is a member of the Therapeutics Advisory Council of Harvard Medical School. He received an A.B. in history from Harvard College, an M.D. from Harvard Medical School, and an M.B.A. from Harvard Business School, where he was a Baker Scholar and won the Loeb Fellowship in Finance.

Tim Haines, Partner, Abingworth LLP. Tim Haines has served as a member of the board of directors since 2014. Mr. Haines joined Abingworth in 2005 and is currently a partner. From 2000 to 2005, he was Chief Executive of Astex Therapeutics, an Abingworth portfolio company. From 1993 to 2000, Mr. Haines was Chief Executive of two divisions of the publicly-listed medical technology company, Datascope Corp. Prior to Datascope, he held a number of other senior management positions in the U.S. and Europe, including CEO of Thackray Inc. and General Manager, Baxter UK. Current and past board positions include Astex Pharmaceuticals, Chroma, Fovea, Pixium Vision, PowderMed, Kspine, Stanmore Implants, Lombard Medical, Sientra, and XCounter. Mr. Haines received a B.Sc. from Exeter University and an M.B.A. from INSEAD.

**Dmitry Kobyzev, Ph.D.** Investment Manager, Inbio Ventures. Dmitry Kobyzev, Ph.D., has been a member of the board of directors since 2014. Dr. Kobyzev joined Inbio Ventures, a venture capital management company representing Pharmstandard International, S.A., in 2014 and is an Investment and Portfolio Manager. From 2010 to 2014, he served as an Investment Director of one of the top Russian life science venture capital teams at RUSNANO OJSC, which has approximately \$1 billion under management. From 2005 to 2010, Dr. Kobyzev advised international private equity and Russian corporate clients within the transactions practice at PricewaterhouseCoopers Russia. Dr. Kobyzev received a Ph.D. degree in economics from Moscow State University.

**Brendan M. O'Leary, Ph.D.** General Partner, Prism VentureWorks. Brendan M. O'Leary, Ph.D., has been a member of the board of directors since 2006. Dr. O'Leary joined Prism VentureWorks, a venture capital firm, in 2003 and is currently a general partner. Dr. O'Leary began his professional career with numerous operating roles at IGEN International, a medical diagnostics company (acquired by Roche), where he served from 1999 to 2003, and Meso Scale Discovery, a high-throughput drug discovery start-up, where he served from 1999 to 2003. Dr. O'Leary received a Ph.D. in organic chemistry from the Massachusetts Institute of Technology and a B.A. in chemistry and economics from Middlebury College, and was a Kauffman Fellow.



**Gregory D. Phelps** Chairman of the Board; Partner, Red Sky Partners. Gregory D. Phelps has been a member of the board of directors since 2008 and has served as chairman of the board since 2009. Mr. Phelps is an independent advisor to biotechnology and pharmaceutical companies. He was a founder and Partner of Red Sky Partners LLC, an advisory firm providing corporate development, product strategy and leadership support to life sciences companies, from 2009 to 2014. Prior to that, Mr. Phelps served as Chairman and Chief Executive Officer of RenaMed Biologics, Inc., a private biotechnology company developing a therapeutic treatment for Acute Kidney Injury, from 2004 to 2007.

Mr. Phelps' previous executive management roles include Chief Executive Officer of Ardais Corporation (2002-2003), Vice Chairman and member of the executive committee of Dyax Corporation (1998-2002), Executive Vice President and Senior Vice President of Genzyme Corporation (1991-1997), Chief Executive Officer of Viagene, Inc. (1988-1990), Chief Executive Officer of ZymoGenetics, Inc. (1986-1988) and various management positions with Baxter Travenol Laboratories, Inc., now Baxter International, Inc. (1975-1986), most recently as Vice President. Mr. Phelps' previous board directorships include Charles River School (2004-2011, board chairman 2008-2011), EPIX Pharmaceuticals Inc. (2004-2009), Ostex International Inc. (1995-2001), Atlantic Biopharmaceuticals, now Merrimack Pharmaceuticals Inc. (1998-2000), Neozyme II Corporation (1992-1996), Genzyme Transgenics Corporation, now rEVO Biologics (1993-1995) and the Hemophilia Foundation of California (1982-1984). Mr. Phelps received a B.S. in electrical engineering from Bradley University and an M.B.A. from Harvard Business School.

Source: Company website

# FIGURE 25. PRTO Income Statement

Proteon Income Statement	2012A	2013A	1-2Q14A	3Q14E	4Q14E	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E
Product Sales and Royalties																	
PRT201 - US Sales			\$ -	\$ -	\$ -	\$ -	\$ -	\$ -	\$ -	\$ 91.2	\$ 141.6	\$ 127.0	\$ 202.2	\$ 376.7	¢ 400 4	\$ 560.4	\$ 580.0
PRT201 - US Sales PRT201 - EU Sales			φ -	φ -	φ -	φ -	φ -	φ -	φ -	φ 91.Z	89.2	133.2	192.8	259.8	445.6	593.3	658.4
Total Sales	+	<del></del>			<u>-</u>			-		91.2	230.8	260.2	395.0	636.5	943.7	1,153.7	1,238.4
PRT201 - JPN Royalties						_	_	_	_	0	200.0	3.4	4.1	6.1	8.1	14.3	18.
Total Revenues	_		_	_		_	_	_	_	91.2	230.8	263.5	399.1	642.6	951.8	1.168.0	1,256.
% change								_		31.2	230.0	203.3	333.1	042.0	331.0	1,100.0	1,230.
Research and development	5.9	4.0	2.8	1.9	1.9	6.6	22.3	43.5	86.97	120.02	144.02	158.42	177.44	195.18	214.70	234.02	252.7
% change	5.9	49.7%	2.0	1.9	10.0%	53.6%	330.4%	60.0%	35.0%	35.0%	65.0%	10.0%	30.0%		35.0%	20.0%	15.09
% net revenue		49.776			10.078	33.078	330.470	00.078	30.078	155%	77%	75%	57%	41%	32%	29%	309
Operating Profit (Loss)	(8.0)	(7.1)	(4.4)	(3.4)	(3.6)	(11.4)	(29.5)	(55.1)	(102.6)	(60.8)	24.3	35.6	128.5	316.6	552.1	709.8	754.
Margin(%)	(0.0)	(,	()	(0. 1)	(0.0)	(,	(=0.0)	(00.1)	(102.0)	-66.7%	10.5%	13.5%	32.2%	49.3%	58.0%	60.8%	60.19
Investment Income	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.2	0.3	0.
Interest Expense	0.0	(0.9)	(0.9)	(0.9)	(0.9)		(3.4)	0.0	0.0	0.0	0.0	0.0	0.0	0	0.2	0.0	
Other income (expense)	0.0	0.1	(0.1)	(5.5)	(0.0)	(0.1)	-										
Total other income	0.0	(0.8)		-	-	(1.0)	(3.39)	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.2	0.3	0.
Pretax income	(8.0)		(5.4)	(4.2)	(3.6)	(13.2)	(29.5)	(55.0)	(102.5)	(60.8)	24.3	35.6	128.5	316.7	552.2	710.1	755.
Provsion for income taxes	` '	` '	` '	\ /	,	-	-	-	-	-	3.6	8.9	45.0	110.8	193.3	248.5	264.
% Tax Rate						0.0%	0.0%	0.0%	0.0%	0.0%	15.0%	25.0%	35.0%	35.0%	35.0%	35.0%	35.0%
Net profit (loss) and comprehensive income	(8.0)	(7.9)	(5.4)	(4.2)	(3.6)	(13.2)	(29.5)	(55.0)	(102.5)	(60.8)	20.6	26.7	83.6	205.9	358.9	461.6	490.
After Tax Margin(%)										-66.6%	8.9%	10.1%	20.9%	32.0%	37.7%	39.5%	39.1
Accretion of redeemable convertible																	
preferred stock to redemption value	(6.1)	(6.1)	(3.4)														
Net profit (loss) attributable to common stockholders	(14.1)	(14.0)	(8.8)	(4.2)	(3.6)	(13.2)	(29.5)	(55.0)	(102.5)	(60.8)	20.6	26.7	83.6	205.9	358.9	461.6	490.
Basic shares outstanding	0.9	4.6	6.8	12.9	12.9	12.9	12.9	13.1	13.4	20.1	20.5	20.9	21.3	21.8	22.2	22.7	23.
Diluted shares outstanding	0.9	4.6	6.8	12.9	12.9	12.9	12.9	13.1	13.4	20.1	21.5	22.0	22.4	22.9	23.3	23.8	24.
Basic GAAP EPS	\$ (9.22)	\$ (1.73)	\$ (1.30)	\$ (0.33)	\$ (0.28)	\$ (1.02)	\$ (2.29)	\$ (4.19)	\$ (7.65)	\$ (3.02)	\$ 1.01	\$ 1.28	\$ 3.91	\$ 9.45	\$ 16.16	\$ 20.37	\$ 21.2
Diluted GAAP EPS	\$ (9.22)			\$ (0.33)	\$ (0.28)			\$ (4.19)	\$ (7.65)		\$ 0.96	\$ 1.22	\$ 3.73	\$ 9.00	\$ 15.39	\$ 19.40	\$ 20.2

Source: Company filings and JMP Securities LLC





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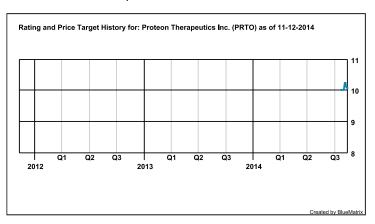
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		# Co's	%		# Co's	%	# Co's Receiving IB Services in	% of Co's
	Regulatory	Under	of	Regulatory	Under	of	Past 12	With This
JMP Rating	Equivalent	Coverage	Total	Equivalent	Coverage	Total	Months	Rating
MARKET OUTPERFORM MARKET PERFORM	Buy Hold	285 142	60.90% 30.34%	Buy Hold	285 142	60.90% 30.34%	103 15	36.14% 10.56%
MARKET UNDERPERFORM COVERAGE IN TRANSITION	Sell	2 36	0.43% 7.69%	Sell	2 36	0.43% 7.69%	0	0% 0%
TOTAL:		468	100%		468	100%	120	25.64%

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