Zacks Small-Cap Research

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Rockwell Med (RMTI-NASDAQ)

RMTI: Q3 Expenses Jump. Calcitriol Launch Pushed Back Again

Current Recommendation	**Underperform**
Prior Recommendation	Neutral
Date of Last Change	09/13/2012
Current Price (11/09/12)	$6.39
Six-Month Target Price	**$4.00**

OUTLOOK

We feel there is significant risk that Rockwell's revenue will remain relatively flat to only slightly positive through 2015. We currently model Calcitriol to launch next year but believe management's sales expectations for their vitamin D analogue product may prove to be wildly optimistic. Our ~$4 million in modeled SFP revenue in 2015 is already risk-adjusted for what we believe to be material aggregate risk encompassing potential for; delays in the clinical trials/data analysis/regulatory filing/FDA turnaround, failure to hit efficacy endpoints, failure to gain FDA approval, less than compelling ESA sparing, and (assuming approved and launched) a strong competitive headwind. If the substantial R&D spend does not produce positive ROI in relatively short-order, shareholder value could be significantly impaired. Our DCF-generated valuation implies fair-value of about $4.00/share.

SUMMARY DATA

52-Week High	**$11.75**
52-Week Low	**$6.33**
One-Year Return (%)	**-5.78**
Beta	**0.92**
Average Daily Volume (sh)	**72,221**
Shares Outstanding (mil)	**21**
Market Capitalization ($mil)	**$136**
Short Interest Ratio (days)	**22.48**
Institutional Ownership (%)	**23**
Insider Ownership (%)	**23**
Annual Cash Dividend	**$0.00**
Dividend Yield (%)	**0.00**
5-Yr. Historical Growth Rates	
Sales (%)	**3.3**
Earnings Per Share (%)	**N/A**
Dividend (%)	**N/A**
P/E using TTM EPS	**N/A**
P/E using 2012 Estimate	**N/A**
P/E using 2013 Estimate	**N/A**
Zacks Rank	**N/A**

Risk Level	**Average,**
Type of Stock	**Small-Growth**
Industry	**Med Products**

ZACKS ESTIMATES

Revenue
(in millions of $)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2011	13.3 A	11.8 A	12.0 A	11.9 A	49.0 A
2012	12.0 A	12.1 A	12.7 A	12.0 E	48.8 E
2013					48.6 E
2014					50.4 E

Earnings per Share
(EPS is operating earnings before non recurring items)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2011	-$0.17 A	-$0.26 A	-$0.28 A	-$0.49 A	-$1.21 A
2012	-$0.54 A	-$0.58 A	-$0.84 A	-$0.27 E	-$2.23 E
2013					-$1.17 E
2014					-$0.74 E

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

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WHAT'S NEW…

Q3 2012 RESULTS / CONFERENCE CALL

Rockwell reported results for Q3 ending September 30, 2012 on November 8th. Aside from the 6% revenue growth, financial results were significantly worse than we had expected. Comments on the conference call and in the 10-Q also implied that the Calcitriol launch will again be pushed back, further reinforcing our concerns related to consistent and ongoing delays in product development and commercialization. And although maybe only a nuance, management's language on the call relative to the expected completion dates of the CRUISE studies suggest this is also being pushed back again.

In summary, there was nothing in the earnings release, in the 10-Q (filed last night) or on the conference call that allayed any of our concerns that we first outlined in our September 14, 2012 initiation report or sways our Sell recommendation. While the shares are down about 25% since we initiated coverage about two months ago we feel stock still trades richer than warranted given the various and significant risks. We are maintaining our Sell recommendation and $4.00/share target price.

Q3 Financials
Revenue of $12.7 million was up 6% yoy, up 5% sequentially and about 4% ahead of our $12.2 million estimate. Despite the slight beat on revenue, gross profit was about 2% lower than our number as a result of softer than estimated gross margin (13% A vs. 13.9% E). SG&A expense jumped in the quarter to $3.3 million, up $1MM (+46%) from Q3 2011, up $500k (+18%) from Q2 2012 and significantly higher than our $2.8 million estimate. R&D expense skyrocketed to $16.3 million, up $5.3 million sequentially and almost $6.5 million higher than our $9.8 million estimate. Management pointed out that they had previously guided that R&D expense would peak in Q3 and attributed the relatively large spend to faster enrollment in their long-term safety study. As such and conceding the benefit of any doubt, we have significantly trimmed our R&D expense for Q4 (from $9.7MM previously to $4.6MM currently). If, however R&D expense does not come down well below $6 million in Q4 our questions and concerns would be further piqued.

Net loss and EPS came in at $17.9 million and ($0.84), well below our $10.8 million and ($0.51) estimates.

Cash
Rockwell exited Q3 with $11.3 million in cash and equivalents, down from $20.4 million at the end of Q2. Given the $17.9 million loss, the $8.8 million cash burn was relatively moderate and benefitted from Rockwell accruing about $3.9 million in R&D liabilities, A/P increasing by $1.7 million and $2.0 million of non-cash share based compensation in the quarter. The $8.1 million and $14.7 million in current A/P and accrued liabilities, respectively, will presumably come due in the very near term and combined with an average quarterly operating cash burn of ~$9 million, Rockwell's $11.3 million cash balance (as of 9/30/12, which may be closer to $6 million today) will not get them very far.

Management again did not provide specifics relative to their plans for raising additional capital but did again allude to the possibility of licensing ex-U.S. rights to SFP. And also noted that they are working on other potential business development activities and other possibly alternatives to address their cash needs. Clearly they need to raise cash very soon.

Product Development Update
As we noted, we think the language on the conference call (and in the 10-Q) indicates the Calcitriol launch is again delayed as well as the expected completion of the SFP CRUISE studies.

Relative to Calcitriol, management's most recent launch guidance prior to the Q3 call was for a launch (per the Q2 call) "in the first quarter of 2013". Yesterday's Q3 conference call management noted that they now expect to be manufacturing their stability batch next week, submit that data to the FDA 30 days later, hope to have manufacturing approval by the end of Q1 2013 and expect to launch immediately afterwards (i.e. - not until Q2). The 10-Q language (which changed from "early 2013" previously to "first half of 2013" with the current 10-Q) also clearly leans towards another delay.

Relative to completion of the CRUISE studies, management had most recently (prior to the Q3 call) guided towards completion in "mid-2013", the Q3 call they point towards August 2013. Again, maybe a nuance but maybe not.

Management still guides towards an NDA filing for SFP by year-end 2013 which we maintain is a best-case scenario, particularly if the trials' completion dates are being pushed back again from prior expectations.

BACKGROUND

Rockwell Medical Technologies, Inc., headquartered in Wixom, Michigan, is one of the largest manufacturers and providers of hemodialysis concentrates. The company's base business, hemodialysis concentrate solutions and dialysis kits, still generates almost $50 million in revenue but has recently been slipping on the top-line and in margins, largely as a result of adverse changes to healthcare reimbursement.

Rockwell's focus for growth lies in two pipeline products, both of which target the hemodialysis market and, assuming eventual regulatory approval, could potentially be seamlessly integrated into their already well-established sales, marketing and delivery infrastructure and sold to their existing customer base. Both of Rockwell's pipeline candidates, soluble ferric pyrophosphate (SFP) and Calcitriol, could benefit from recently implemented changes by Medicare for hemodialysis reimbursement which should increase demand for lower cost hemodialysis services, drugs and supplies. Management has high hopes for both product candidates but particularly SFP, a novel late-stage soluble iron supplement which aims to replace intravenous iron (IV iron) as the industry standard therapy for anemic hemodialysis patients.

Based on the potential for SFP to reduce dialysis costs (thereby maximizing profit for providers) and lower the adverse event risk compared to IV iron therapy, management expects strong demand for SFP at the outset of commercialization. This, coupled with being able to leverage their established distribution and customer base, offers the possibility of rapid revenue growth and almost immediate margin expansion. Rockwell hopes to launch SFP in the U.S. by sometime in 2014 but first must gain FDA approval. While SFP phase II clinical data, which was first announced in early 2010, showed a very strong safety profile, efficacy was, in our opinion, less than compelling. Rockwell subsequently moved the candidate into phase III trials, which consist of two identical 300-patient studies (CRUISE I and CRUISE II) which will support the FDA regulatory filing and PRIME, a (non-FDA) 100-patient marketing study powered to demonstrate that SFP can reduce the amount of ESA required to maintain hemoglobin in patients undergoing hemodialysis. Management expects CRUISE I/II to complete in August 2013 and hopes to file an NDA in Q4 2013. Assuming all goes to plan and a ~12-month turnaround by FDA, this could put SFP on the U.S. market sometime in late 2014.

Rockwell believes their other pipeline candidate, Calcitriol, a generic injectable vitamin D analogue which also targets the chronic renal failure market, could launch in Q2 2013. As the drug is already FDA-approved, RMTI only needs manufacturing stability data approved by the agency in order to begin commercialization. Rockwell expects their Calcitriol product to receive a warm welcome given its lower price-point relative to branded vitamin D analogues in the face of the recent Medicare reimbursement changes.

HEMODIALYSIS

The kidneys of end-stage renal disease patients no longer function properly and therefore these individuals must undergo regular dialysis to keep them alive. Hemodialysis is a process whereby an extracorporal (i.e. - outside the body) device removes waste products from the blood of patients with severely compromised kidney function including those with chronic kidney disease (CKS) and end stage renal disease (ESRD). We estimate that there are approximately 500k people in the U.S. with ESRD receiving hemodialysis. Rockwell Medical targets the hemodialysis market through the sale of dialysate concentrates and hopes to have their novel soluble iron supplement on the market in 2014.

Dialysate Concentrates

About 94% of RMTI's current revenue is derived from the sale of their hemodialysis concentrates and solutions. Hemodialysis concentrates are solutions which are mixed with water and form the dialysate which is pumped in the opposite direction of the blood through the dialyzer and carries away waste products and excess water from the blood. The market for hemodialysis concentrates and solutions is estimated at about $185 million annually and is highly concentrated with German company Fresenius Medical and Denver-based DaVita Inc. estimated to hold combined share of about 65%. Fresenius and DaVita are two of the largest dialysis clinic owners and operators, which source a significant portion of the hemodialysis concentrates and IV iron. Rockwell's ~$46MM in

dialysate concentrate revenue represents about 27% share of this market, which includes about $23 million in revenue from sales to DaVita, Rockwell's largest customer.

Iron Supplementation
Patients undergoing chronic hemodialysis often suffer from iron deficiency due to iron left in the dialysis circuit and frequent phlebotomies. Lack of iron, coupled with reduced erythropoietin production from the damaged kidneys, makes ESRD patients susceptible to anemia, a decrease in the number of red blood cells, and a decrease in hemoglobin. Hemoglobin carries oxygen from the lungs throughout the body and is essential for the body to create energy and maintain normal functions. In order to maintain hemoglobin levels, hemodialysis patients are often given iron supplements along with erythropoiesis stimulating agents.

Erythropoiesis stimulating agents (ESA) are manmade versions of naturally-produced erythropoietin (EPO), which is a hormone produced in the kidneys and is a key component for the production of red blood cells. While ESA's, which are administered by injection, are effective at increasing the production of red blood cells, they have certain drawbacks such being relatively expensive and associated with serious cardiovascular risks. As such, providers have an interest in limiting the ESA dose. Studies have shown that hemoglobin response can be maintained with lower ESA dose when supplemented with IV iron.

IV iron is given during the hemodialysis procedure. The IV iron market specific to ESRD is estimated at roughly $400 million/year. There are currently five IV iron products on the market in the U.S. including INFeD and DexFerrum (both iron dextrans), Venofer (iron sucrose), Ferrlecit (sodium ferric gluconate), and Feraheme (ferumoxytol). While there has been no rigorous head-to-head clinical studies done comparing efficacy and safety among the different IV iron therapies, the general consensus among hematologists seems to be that there is no clear differentiation relative to efficacy but there is (at least) some difference with regard to safety.

Iron dextran became available in the 1950's but went out of favor since the introduction of newer IV iron supplements with more favorable safety profiles (iron dextran can cause anaphylactic reactions), namely sodium ferric gluconate, iron sucrose and ferumoxytol. These newer IV iron products have all demonstrated relatively strong safety profiles, although some risks are present, mostly associated with the carbohydrate shell which slows the release of iron (slower release reduces risk of toxicity related to free iron). Sodium ferric gluconate and iron sucrose have been associated with adverse reactions due to the release of free iron, including anaphylactic reactions, but at a much lower incidence than iron dextran. The newest of the IV iron therapies, ferumoxytol, was approved by the FDA in 2009 and is surrounded by a shell which allows a relatively large amount of iron to be delivered relatively rapidly. The advantages of this dosing seem to be more obvious with non-dialysis patients where IV access is limited - with dialysis patients, vascular access is already done during the dialysis session (3x/week) so longer administration of lower doses is easily and conveniently accomplished. While the carbohydrate shell has been associated with certain adverse reactions (most commonly hypotension), clinical studies in dialysis patients demonstrated a safety profile similar to or better than oral iron.

Relative to the safety profiles of the newer (i.e. - excluding the high molecular weight dextrans), a paper authored by doctors at the Georgetown University School of Medicine and New York University School of Medicine concluded that, "Until reliable comparative data becomes available, one product cannot, and should not, be considered superior in terms of safety profile."[1]

The IV iron market relative to ESRD is currently mostly dominated by Venofer (Vifor Pharma) with Ferrlecit (Sanofi-Aventis) having significantly less market share. Venofer benefits from Vifor's partnership with Fresenius (Vifor Fresenius Medical Care Renal Pharma) which uses Venofer in its vast network of dialysis clinics. Feraheme (AMAG Pharmaceuticals) has yet to make much of a dent in the ESRD space as it's most widely used in non-dialysis patients.

SOLUBLE FERRIC PYROPHOSPHATE (SFP)

Soluble ferric pyrophosphate is Rockwell's lead pipeline candidate which management expects to be the long-term value driver of the company. SFP is being developed as a replacement for IV iron as the industry standard therapy for anemic hemodialysis patients. Unlike IV iron, which is typically administered over a few minute period during a dialysis session and must be processed by the liver before it's transferred into the blood plasma, SFP is delivered

[1] *Clinical Use of Intravenous Iron: Administration, Efficacy, and Safety*, Michael Auerbach and Harold Ballard, Georgetown University School of Medicine and New York University School of Medicine

with the dialysate directly into the blood plasma. The proposed benefits being that SFP will maintain a more even iron balance in the body which may improve ESA-iron response (thereby reducing the amount of required ESA, which is costly and has safety risks) and, since it bypasses the liver, will not cause adverse reactions associated with IV iron such as inflammation/oxidative stress. RMTI also notes that the administration advantage of SFP over iron can reduce the amount of nursing time and associated cost.

PHASE IIa STUDY

SFP was evaluated in a small, single-site, open-label, six-month dose-escalating study to determine safety, effectiveness and optimal dose of SFP. The study enrolled 21 hemodialysis patients, all of which were stabilized on IV dextran iron. The treatment arm consisted of 10 patients which received escalating doses (2, 4, 6, 8, 12 ug Fe/dL dialysate) of SFP while the 11 patients in the control arm continued receiving dextran iron. Results showed both groups maintained hemoglobin levels consistent with baseline, demonstrating that SFP effectively maintains hemoglobin in the absence of IV iron therapy. SFP at 12 ug Fe/dL dialysate was considered to be the optimal dose. The study also showed SFP, which was dosed 700 times during the trial, was safe.

PHASE IIb STUDY

RMTI subsequently moved into a larger phase IIb study which completed in 2009. The six-month, double-blind, dose-ranging study enrolled 131 ESRD patients on hemodialysis at 29 trial sites in the U.S. and Canada to determine safety, effectiveness (ability to maintain iron levels) and optimal dose of SFP.

The primary efficacy measure was the percent of subjects whose hemoglobin (Hgb) decreases by a total of 1.0 grams/deciliter (g/dL) (or more) from baseline on each of two successive measurements for up to 26 weeks (6 months). Hemoglobin was obtained weekly at the mid-week dialysis treatments and compared to baseline value (average of two Hgb measurements obtained at the two consecutive baseline visits prior to randomization).

ESRD patients receiving chronic hemodialysis were randomized to dialysate with no iron (control) or dialysate with SFP at one of four SFP doses (5, 10, 12, 15 ug Fe/dL dialysate). Randomization results were; 26 patients @ 0 ug iron/dL, (control), 26 patients @ 5 ug iron/dL, 29 patients @ 10 ug iron/dL, 22 patients @ 12 ug iron/dL, and 28 patients @ 15 ug iron/dL.

While Safety Looked Good…

The 105 SFP treated patients received an aggregate 4,882 treatments using a total of over 700k liters of dialysate. Similar to the phase IIa study, the IIb study showed SFP was well-tolerated with no SFP-related toxicity. The incidence of serious adverse events was higher in the placebo (control) group (7 of 26 = 26.92%) than the combined treatment group (19 of 105 = 18.10%) as was the incidence of other (non-serious) adverse events (placebo: 20 of 26 = 76.92%, combined treatment: 70 of 105 = 66.67%).

…Efficacy Was Less Than Compelling…

The primary efficacy endpoint of the study, a decrease in Hgb of 1.0 g/dL or more from baseline on each of two successive measurements, didn't even come close to being met. Statistical analysis comparing control with SFP patients at each dose at a 95% confidence interval resulted in a range of p-values from 0.299 to 0.999. Only 5% of placebo patients experienced a decrease in Hgb of 1.0 g/dL or more from baseline compared to 6% (p-value 0.999) of patients @ 5 ug iron/dL, 5% (p-value 0.807) of patients @ 10 ug iron/dL, 4% (p-value 0.748) @ 12 ug iron/dL, and 10% (p-value 0.299) patients @ 15 ug iron/dL.

Primary Endpoint: % of subjects whose Hgb decreases by a total of 1.0 g/dL or more from baseline on each of two successive measurements

	0 µg Iron/dL of Dialysate	**5 µg** Iron/dL of Dialysate	**10 µg** Iron/dL of Dialysate	**12 µg** Iron/dL of Dialysate	**15 µg** Iron/dL of Dialysate
Number of Participants Analyzed [units: participants]	26	26	29	22	28
Percent of Subjects Whose Hemoglobin (Hgb) Decreases by a Total of 1.0 Grams/ Deciliter (g/dL) (or More) From Baseline on Each of Two Successive Measurements. [units: Percent of subjects]	5	6	5	4	10
Placebo vs. respective dose p-value @95% C.I.		0.999	0.807	0.748	0.299

SOURCE: clinicaltrials.gov

Management surmised that the reason for this were certain trial protocol violations that happened by chance along with control patients being more iron-loaded. Specific to iron-loading, over the two months leading into enrollment of the study, average IV iron supplementation of control group patients was substantially more (32% more: 466mg control vs. 354mg avg. treatment - see table below) than that of SFP patients which presumably would have resulted in relatively higher levels of stored iron in control patients. These iron stores, per Rockwell, then sustained Hgb levels in control patients throughout the 26-week term of the study, causing the endpoint to be missed. This is a theory that seems to be at least somewhat feasible given the baseline/lead-in data but the study did not produce any scientific evidence that this was the likely reason for the endpoint being missed. We also point out that baseline ferritin levels of the control group (510 ug/L) were lower than both the average (558 ug/L) of all the treatment groups as well as each individual treatment group. While all ferritin and TSAT levels were well within the trials' inclusion criteria, in the context of accepting that the differences in amounts of lead-in iron could have skewed the results in favor of control, we think it's reasonable to concurrently accept that differences in baseline ferritin levels could have skewed the results in favor of the treatment groups (albeit with potentially less impact). We also acknowledge that the difference in control vs. average treatment ferritin of 9% was relatively benign. To be clear, we are not theorizing that the differences in baseline ferritin necessarily had any impact on the endpoint, but offer that this, similar to the lead-in iron argument, is just a supposition at this point with no clear evidence supporting that it had any significant effect on the outcomes data.

Phase IIb Control and Treatment Patient Baseline/Lead-In Characteristics

Parameter (Mean or %)	Placebo N=26	SFP 5 µg/dL N=26	SFP 10 µg/dL N=29	SFP 12 µg/dL N=22	SFP 15 µg/dL N=28	All SFP Groups Combined N=105
Hgb (g/dL)	11.1	11.1	11.0	10.9	11.3	11.1
CHr (pg)	32.6	33.0	32.9	32.3	32.6	32.7
Ferritin (µg/L)	510	564	542	534	591	559
TSAT (%)	26.7	27.8	28.1	26.4	26.1	27.1
Serum Iron (µg/dL)	59.1	58.7	60.0	57.3	53.1	57.2
IV iron in the 2 months prior to screening (mg)	466	291	394	411	321	352
Epoetin dose (U/week)	(N=21) 15,024	(N=20) 15,815	(N=23) 19,926	(N=18) 21,872	(N=23) 14,504	(N=84) 17,880
Darbepoetin dose (µg/week)	(N=5) 58.8	(N=6) 39.0	(N=6) 49.2	(N=4) 42.3	(N=5) 58.8	(N=21) 47.2

SOURCE: Poster: Reduced ESA Requirement by Continuous Delivery of SFP via Dialysate in CKD-HD Patients. Rockwell Medical

The protocol violations relate to ESA dosing changes from baseline and some patients receiving IV iron during the trial, both of which RMTI believes could confuse the outcome data. Per the study protocol ESA dosing was to remain static throughout the study. RMTI noted that in 29% of patients that that didn't happen - specifics relative to how many patients in which cohorts the ESA changes relate to or the degree and direction of all the changes were not released - although the company did note that in the combined SFP cohort, 18% of ESA changes were reductions (including a 31% dose reduction in SFP 10 group) compared to 11% in the control group. RMTI implied (in company press releases and presentations) that some of the SFP treated patients required a decrease in ESA dosage due to Hgb rising too quickly. RMTI also noted 15% of placebo patients received IV iron during the study - another violation of the study protocol.

Secondary Endpoint Met

While a statistically significant change in Hgb from baseline to the final evaluation (up to 26 weeks), a secondary endpoint, was met (although just barely) at the 10 ug iron/dL dose (p-value 0.049 @ 95% C.I), it handily missed at every other dose. The data also does not indicate an obvious dose-dependent response of SFP on hemoglobin. Protocol violations were also implicated for this less-than compelling evidence of SFP's effectiveness and lack of a clear dose response.

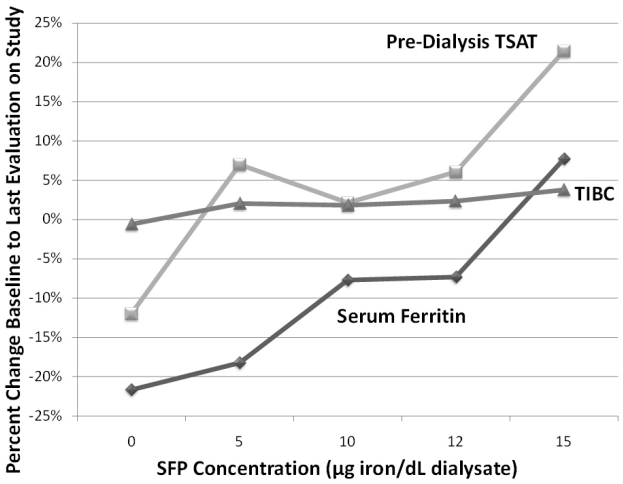
Secondary Endpoint: Change in Hgb from baseline to final evaluation

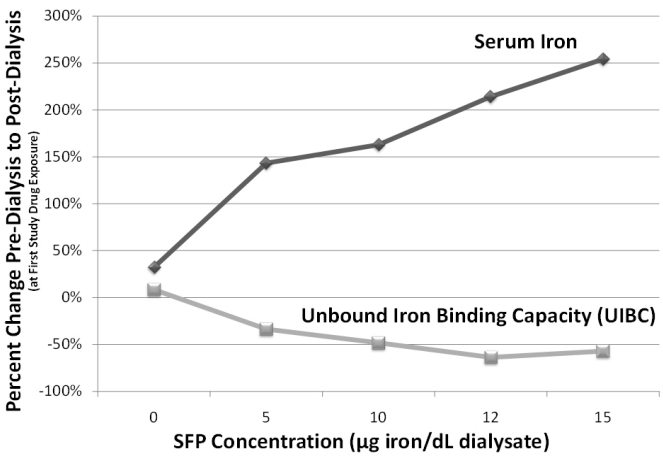
	0 µg Iron/dL of Dialysate	5 µg Iron/dL of Dialysate	10 µg Iron/dL of Dialysate	12 µg Iron/dL of Dialysate	15 µg Iron/dL of Dialysate
Number of Participants Analyzed [units: participants]	26	26	29	22	28
Change From Baseline in Hemoglobin (Hgb) [units: grams/ deciliter (g/dL)] Mean ± Standard Deviation	-0.177 ± 1.1151	0.258 ± 1.4643	0.462 ± 1.2214	0.173 ± 1.5806	-0.018 ± 1.2532
Placebo vs. SFP respective dose p-value @ 95% C.I.		0.234	0.049	0.375	0.625
Mean change in Hgb (g/dL), SFP respective dose less placebo		0.435	0.639	0.350	0.159

SOURCE: clinicaltrials.gov

Despite the primary endpoint being missed and a lack of dose response of SFP on hemoglobin in the phase IIb trial, RMTI decided to move SFP into phase III trials. The rationale was that had it not been for the protocol violations caused by faults in the study design, the primary endpoint would have been met and, per management, based on "surrogate endpoints", namely changes in serum iron and unbound iron binding capacity (UIBC), there in fact was "overwhelming evidence of dose-dependent SFP derived iron transfer and uptake."[2]

While we agree that the data does indicate a dose-dependent response on iron transfer (in terms of a change in serum iron, transferrin saturation and ferritin - see charts below), there's no obvious consequential reaction on the production of hemoglobin, which is the end goal of iron supplementation with hemodialysis associated anemia. Essentially what this means is that while SFP appears to work relative to getting the iron from the dialysate into the patient's blood and even to increase iron stores, there's no strong evidence that suggests it facilitates the final process, which brings into question its worth in its targeted therapy. So management's claim that "Serum iron parameters provide compelling evidence of dose-dependent patient exposure to SFP and serve as surrogate markers showing efficacy" [2], is, in our opinion, only partially supported by the clinical data to-date. The implication in that statement that these surrogate markers show efficacy in maintaining hemoglobin levels certainly does not seem to be supported by the clinical data.





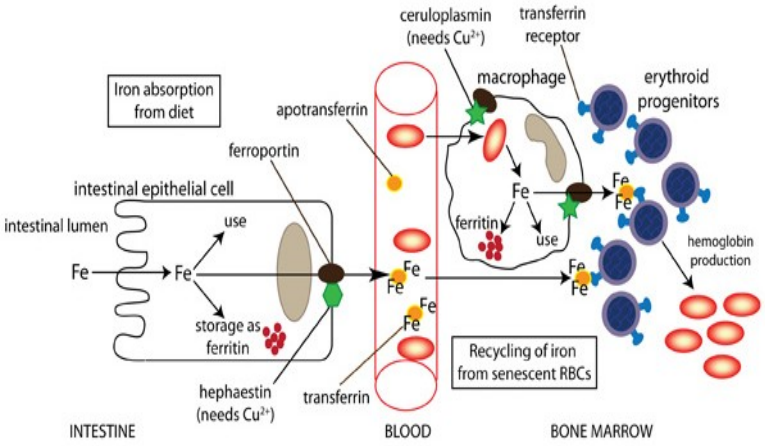
SOURCE: Rockwell Medical

In addition to differences in iron-loading and protocol violations potentially contributing to the primary endpoint being missed, Rockwell opines that it's also possible the higher doses of SFP actually worked too well at

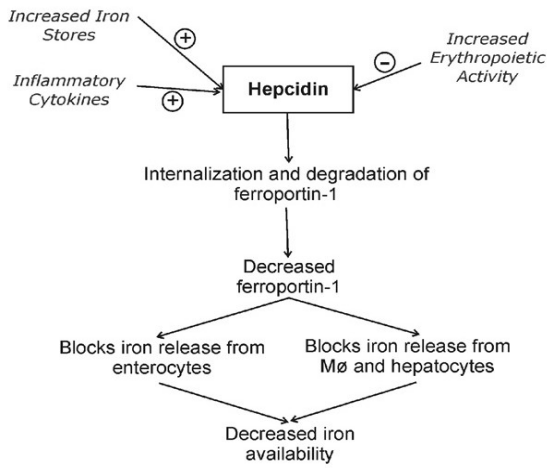
[2] *Rockwell Medical Announces Positive Phase IIb Clinical Data*, Rockwell Medical/Global Newswire via COMTEX News Network, February 25, 2010

increasing patients' iron levels which in-turn triggered an iron-withholding response by the body. Specifically, Rockwell believes that the higher doses of SFP (12 ug iron/dL and 15 ug iron/dL) increased iron to levels which triggered the body to increase hepcidin and resulted in reticuloendothelial block (RE block). Hepcidin is produced by the liver and regulates iron transport in the intestines, working to prevent excess iron absorption in the digestive tract and maintaining normal iron levels in the body. Hepcidin was just discovered about ten years ago. What triggers the body to regulate levels of the hormone is still not yet fully understood but it's believed that stored iron levels, inflammation, and erythropoiesis activity can all influence hepcidin. Rockwell believes that higher SFP doses caused hepcidin levels to increase as a result of either a direct response to higher iron levels or due to an inflammation response to too much iron (too much iron is toxic). Elevated levels of hepcidin can result in RE block whereby absorption of dietary iron into the gastrointestinal tract and release of stored iron into plasma (transferrin) is seriously impeded. As hemoglobin synthesis requires transferrin to transport iron to the site (bone marrow) of red blood cell (RBC) production, RE block can cause hemoglobin levels to fall in patients that may have adequate iron stores. Rockwell has cited elevated hepcidin/RE block as potentially being triggered by the higher iron levels associated with SFP at doses 12 ug iron/dL and 15 ug iron/dL.

Iron's Path In Hemoglobin Production



Cause And Effect Of Hepcidin Production



SOURCE: Cornell University

RE Block / Hepcidin Hypotheses Might Be Problematic

We have a problem with the RE block hypothesis, particularly with also mutually accepting that SFP works as RMTI theorizes. The first issue (which in our opinion is by far the least problematic) is the absence of clinical data to support RE block. The change in hepcidin was not measured in phase II nor were certain cytokines (such as interleukin-1 and interleukin-6) related to the body's inflammatory response and believed to be associated with the production of hepcidin. Lacking these measurements doesn't mean RE block / elevated hepcidin didn't occur, it just means that it's a hypothesis without any data supporting it. Used as support for the RE block theory is that serum ferritin did increase (see graph earlier) from baseline to final evaluation (by about 8%) at the highest SFP dose (15 ug iron/dL) - and potentially this increase in serum ferritin triggered RE block - but, again, this is not clear clinical evidence to support RE block.

However, the issue that is particularly problematic is that even if we do assume that RE block occurred at the higher SFP doses, it does not explain why the change in hemoglobin levels of these higher-SFP-dose patients did not meet statistical significance. Remember, one of the most important supposed advantages of SFP relative to IV iron is that it delivers useable iron directly to apo-transferin (the plasma then carries the iron to the bone marrow for hemoglobin synthesis), bypassing the liver (RE system) altogether. The benefits of this method of action is that SFP could deliver useable iron faster (IV iron must be processed by the liver which can take time) and by bypassing the liver, would reduce the risk of oxidative stress on the liver, a common side effect of iron supplementation. By implicating RE block for the lack of SFP's efficacy on the production of hemoglobin seems to first require the assumption that there's a problem with the hypothesized performance of SFP - in particular that maybe SFP-bound transferin is actually not useable (or less effective) iron. Taking this one step further, perhaps it was stored iron, not SFP that was the catalyst for the statistically significant increase in hemoglobin experienced by the 10 ug iron/dL dosed patients. Following that logic and the theory that higher doses of SFP (12 ug iron/dL and 15 ug iron/dL) triggered RE block might also offer a possible explanation to why the change in hemoglobin

levels from baseline in these two higher dose groups was less than that in either of the two lower dose (5 ug iron/dL and 10 ug iron/dL) groups. We note that this scenario is complete conjecture on our part but it is an alternative theory that can not be disproven by the clinical data to-date. We think given the lack of compelling evidence on both sides of the argument that there's sufficient reason to question the reasonableness of the RE block theory while at the same time accepting that SFP's hypothesized method of action and performance relative to the production of hemoglobin is sound.

ESA SPARING

Given the high cost of ESAs and their adverse risk profile, there's an inherent interest in limiting how much is used. Rockwell measured ESA-sparing, or the ability to reduce the ESA dose required to maintain hemoglobin, in the phase IIb study although this was not part of the trial protocol. The company released limited information on the ESA-sparing results but indicated that the phase IIb data showed evidence of ESA-sparing with SFP. The data that was released showed a statistically significant reduction (13% reduction, p-value 0.044, 95% C.I.) in the mean percentage ESA dose change from baseline to final evaluation in the SFP 12 ug iron/dL dose cohort compared to placebo. Rockwell has indicated that dialysis providers consider a reduction as little as 1% in ESA to be meaningful from a cost perspective.

The other SFP dose groups did not demonstrate a statistically significant ESA dose change, although the SFP 5 and 10 groups did show a reduction of ~5%. Rockwell's phase III PRIME (marketing) study is powered to measure ESA-sparing which should give a much more clear indication of SFP's ability to reduce the amount of ESA required - Rockwell believes they may see upwards of 25% ESA sparing in PRIME.

PHASE III STUDIES

Rockwell currently has SFP in phase III trials, consisting of two identical 300-patient studies (CRUISE I and CRUISE II) which will support the FDA regulatory filing and PRIME, a (non-FDA) 100-patient marketing study powered to demonstrate that SFP can reduce the amount of ESA required to maintain hemoglobin in patients undergoing hemodialysis. PRIME completed enrollment earlier in 2012 and is ongoing. The CRUISE studies completed enrollment in late July and management's current expectations are that the studies will complete around August 2013 and Rockwell will file an NDA in Q4 2013. This could potentially put SFP on the market sometime in late-2014.

CRUISE 1 / 2

The CRUISE (Continuous Replacement Using Iron Soluble Equivalents) studies are an extension of the phase IIb study but with some differences in the primary endpoint as well as the protocol, the latter so as to address the protocol violations in the phase IIb study. CRUISE 1 /2 are randomized, placebo-controlled, multi-site studies to confirm the safety and efficacy of SFP in maintaining iron delivery for erythropoiesis in anemic adult patients with chronic kidney disease receiving hemodialysis. Approximately 150 patients in each study will be randomized to either SFP-iron @ 11 ug iron/dL or placebo (standard dialysate with no iron). Treatment duration will be up to 12 months.

Rockwell announced the design of the CRUISE studies, including the primary endpoint, in an October 2012 press release. Interesting is that efficacy will be measured not by the primary endpoint of the phase IIb study (which RMTI did not hit) but instead by the mean change from baseline in Hgb between the SFP group and placebo, which is the same as the secondary endpoint in the phase IIb trial (which was met at the SFP 10 dose).

Certain modifications of the CRUISE design compared to the phase IIb study are expected to mute the protocol violations seen in phase IIb. This includes stopping IV iron administration earlier prior to commencement of the study, longer treatment duration (12 months vs 6 months) and additional measures to reduce changes in ESA dosing.

Both DaVita and Fresenius, two of the largest dialysis organizations, are participating in the phase III trials which not only potentially adds additional credibility to the utility of SFP, it also provides RMTI (assuming FDA approval) with a seamless transition of SFP into the supply agreements already established with DaVita.

PRIME

PRIME is a multi-center, randomized controlled 9-month study in which 100 hemodialysis patients will receive either SFP or standard (no iron) dialysate. IV iron sucrose (Venofer) can be dosed in either group per protocol in cases of iron deficiency. The clinical study design is aimed at demonstrating ESA sparing as well as to examine maintenance of hemoglobin, iron parameters, the need for IV iron, and oxidative stress markers in patients receiving SFP. The objective of the study is to determine whether SFP reduces the requirement for ESAs by

maintaining iron balance. Enrollment completed in late April 2012. RMTI currently expects that top-line results will be available in February 2013.

PRIME is solely a marketing study and results (assuming positive) will be used to support RMTI's marketing efforts, specifically that SFP can reduce the need for ESAs, thereby reducing cost (see our discussion below on changes to Medicare reimbursement) and limiting patient exposure and related risks. Results of PRIME will not have any bearing on FDA approval.

Relative to the economic benefits of ESA-sparing, Rockwell has noted that a 0.5% ESA reduction equates to about $1 in cost reduction per treatment, or approximately $150/year per patient. Per Rockwell, ESA currently costs providers ~ $8k/year per patient. So as an example, if PRIME can show an ESA-sparing of 2%, this would equate to ~$600/year per patient savings for providers or about 7.5%, which providers would almost certainly consider highly significant (RMTI has noted that as little as 1% sparing would be considered significant). And, as noted above, the phase IIb study indicated ESA-sparing could be much greater than this.

If, however, SFP does not demonstrate meaningful ESA-sparing, we think potential demand could be significantly impaired given IV iron's established position as the standard of care. While SFP may offer ancillary benefits over IV iron such as lower administration burden/cost and possibly an advantageous safety profile (a benefit in safety would need to be substantiated over a period of time), these may not provide significant enough switching incentive given the "we know what to expect from the standard of care" mentality and related risk aversion to novel products common with health care providers.

CALCITRIOL

Rockwell acquired an abbreviated new drug application (ANDA) for calcitriol in July 2011 for an undisclosed purchase price. Rockwell believes, Calcitriol, a generic injectable vitamin D analogue which also targets the chronic renal failure market, could launch in Q2 2013. As the drug is already FDA-approved, RMTI only needs manufacturing stability data approved by the agency in order to begin commercialization. Rockwell expects their Calcitriol product to receive a warm welcome given its lower price-point relative to branded vitamin D analogues and Medicare recently bundling (i.e. - effectively reducing) reimbursement. On the Q3 2012 earnings call management noted that they now expect to be manufacturing their stability batch next week (w/e 11/18/2012), submit that data to the FDA 30 days later, and hope to launch immediately afterwards.

ESRD and CKD patients often suffer from a deficiency of vitamin D as a result of the damaged kidneys' inability to convert cholecalciferol (vitamin D3) into its active form, calcitriol. Vitamin D deficiency can lead to low blood calcium and secondary hyperparathyroidism, a condition associated with bone and joint pain as well as limb deformities. As a result, most of these patients receive a vitamin D supplement to reduce the parathyroid hormone. The most common vitamin D supplements used to treat ESRD patients are calcitriol, paricalcitol (*Zemplar*, Abbott), doxercalciferol (*Hectorol*, Genzyme), and cinacalcet (*Sensipar*, Amgen). Calcitriol is sold generically and under various brand names by some major pharmas (including Roche and Abbott), while the others have yet to lose patent protection and are sold only under their respective brands (although a generic Zemplar could hit the market soon).

Hectorol and Zemplar (Zemplar is sold in IV and oral versions) currently dominate the IV vitamin D market, estimated at roughly $350MM - $400MM annually. Sensipar is given orally. There's some debate whether calcitriol is as effective as the competing products. One study (n=263) in particular comparing Zemplar to calcitriol showed Zemplar treated patients achieved a $\geq$ 50% reduction from baseline in parathyroid syndrome significantly faster than calcitriol treated patients (p-value 0.025) and achieved a mean reduction of PTH into a desired therapeutic range (100 to 300 pg/mL) at approximately week 18, whereas the calcitriol-treated patients, as a group, were unable to achieve this range. Safety was also better in the Zemplar treated patients.[3] Clinical studies with Sensipar in secondary hyperparathyroidism indicate it could potentially offer even greater efficacy.

Calcitriol Hopes To Compete On Price

Rockwell's value proposition with their Calcitriol product will stress adequate efficacy with significant cost savings over the competing products, particularly to the higher-priced branded drugs. Until recently cost of injectable vitamin D was not a concern to providers as Medicare provided reimbursement separately from the dialysis

[3] *Paracalcitol versus calcitriol in the treatment of secondary hyperparathyroidism*. NIH. Division of Nephrology/Hypertension and Dpt of Medicine, Northwestern University Feinberg School of Medicine.

procedure (see our discussion below). However, this changed when Medicare bundled reimbursement of dialysis drugs and supplies together with the procedure, thereby incentivizing providers to use lower-cost options. Rockwell is counting on this bundled reimbursement to drive demand for their Calictriol product. While we believe dialysis providers will look for cost-efficient vitamin D analogue options, which could potentially benefit Rockwell's Calcitriol, we also think that it's likely that the prices of competing branded products will be adjusted downward in order to be more price competitive and stem any significant losses in market share. In addition, a generic version of Zemplar could hit the market by 2014 which would likely offer very stiff competition to Calcitriol. This, coupled with clinical evidence indicating potentially superior efficacy and safety of competing products, may significantly limit the potential opportunity of Rockwell's Calcitriol product.

BUNDLED REIMBURSEMENT

The Medicare Improvement for Patients and Providers Act, which was passed in July 2008, included a provision whereby Medicare reimbursement for dialysis bundles the procedure as well as related supplies and drugs together. This is a significant change from the past where the dialysis services were paid separately from the related supplies and drugs, including iron supplements, ESA, and vitamin D analogues. Prior to bundling, providers had a financial incentive to use more dialysis drugs (particularly ESAs and branded vitamin D analogues which are relatively expensive) as they were reimbursed at a rate of cost plus 6%. Bundled reimbursement means the provider is now reimbursed one lump-sum and is therefore incentivized to use more economical options.

Implementation of the bundled payment system began on January 1, 2011 with complete implementation by the end of 2014. Over this 4-year time period, the new bundled payment system will be transitioned "in equal increments" annually as follows: In 2011, 25% of payments; in 2012, 50%; in 2013, 75%; and in 2014, 100%.[4] A base rate of $229.63 per dialysis treatment has been set.

Bundling now places maximum emphasis on cost efficiently maintaining Hgb. A number of solutions to do this have been suggested by various hemodialysis industry participants. Among these are limiting the ESA dose, increasing in-home dialysis (versus in-center), and use of lower cost vitamin D analogues.

Limiting ESA dose is at the forefront, given the high cost of the drugs. The means to do so could come in the form of increasing the use of IV iron, or potentially via more efficient ESA administration schedules. Rockwell believes SFP could benefit from bundled reimbursement as providers look to increase the use of the most cost-effective iron supplements and will be attracted by SFP's lower cost of administration compared to IV iron. While reducing the cost of iron administration may provide meaningful benefit, there are other potentially more substantial alternatives to lower the cost of ESA, including directly reducing the cost of the ESA injections.

The FDA-approved administration schedules of currently available ESAs is three times per week for EPO and once weekly to every two weeks for darbepoetin.[5] Certain studies have shown that hemoglobin targets may be maintained by extending the dosing schedules to every four weeks for darbepoetin and every two weeks to every 4 weeks with novel long-acting erythropoietin receptor activators (CERA). Mircera (methoxy PEG-epoetin B), Roche's CERA drug, is FDA approved and is expected to be available in the U.S. in mid-2014.

Two time and motion studies have been done which demonstrated the potential cost savings associated with fewer ESA injections.[5,6] The studies indicated that administration and patient observational costs could be reduced by up to as much as 80% if three times per week ESA dosing were switched to once per month dosing and between 35% and 58% cost savings if once weekly to three times per week ESA dosing were switched to once per month dosing. Relative to the potential cost savings of once-monthly ESAs, Dr. Chaim Charytan (Renal Division, New York Hospital Medical Center of Queens) notes in his article titled *Bundled-Rate Legislation for Medicare Reimbursement for Dialysis Services: Implications for Anemia Management with ESAs,* that "Time savings gained with use of a once-monthly ESA can provide cost efficiencies in a reimbursement-limited bundling environment. Additionally, they may allow nurses more opportunity to provide quality care focused on overall patient needs (*e.g.*, clinical evaluation, disease management, and patient education)."[5]

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[4] *Bundled-Rate Legislation for Medicare Reimbursement for Dialysis Services: Implications for Anemia Management with ESAs,* CJASN, Dr. Chaim Charytan. Medicare program: ESRD prospective payment system. Final Rule. Fed Regist 75: 49029-49214, 2010

[5] *Costs of managing anemia with erythropoieses-stimulating agents during hemodialysis: A time and motion study*. Schiller B, Doss S, De Cock E, Sapede C. Hemodial Int.

[6] *Healthcare resource utilization for anemia management: Current practice with erythropoieses-stimulating agents and the impact of converting to once-monthly CERA.* Saueressig U, Kwan JTC, De Cock E, Sapede C. Blood Purif

FINANCIAL CONDITION

As of their most recent reporting period (Q3 ending 9/30/2012) RMTI had $11.3 million in cash and investments and no debt. Cash used in operating activities was $8.8 million and $23.6 million in the three and nine months ending 9/30/2012. Stripping out changes in working capital (which includes a $5.6 million spike in A/P and accrued liabilities in Q3), cash used in operations was $15.6 million and $34.5 million over those same periods. CapEx has been minimal.

Excluding R&D expenses, management expects the company to be cash flow positive in 2012. We estimate cash burn will remain at the ~$9 million/quarter run-rate through the completion of the PRIME and CRUISE studies which management has ballparked to wrap up around mid-2013.

The company raised $16.2 million (net) from the sale of common stock in February and another $1.6 million in proceeds from the exercise of warrants during 1H 2012. As of 9/30/2012 RMTI's cash balance represented about 4 months worth of operating capital. Our modeled outstanding share count assumes the company continues to raise additional funds from the sale of equity and through the exercise of warrants.

OUR CONCERNS

- **Weak Phase IIb Efficacy Data**
  The primary endpoint of the phase IIb dosing study, efficacy of SFP in maintaining iron levels as measured by the percentage of subjects whose hemoglobin decreases by 1.0 g/dL or more from baseline on each of two successive measurements (for up to 26 weeks), was not met. In addition and in contrast to management's implications, we do not believe the phase IIb data showed a clear dose response of SFP on change in hemoglobin levels.

  While a secondary endpoint, a change in Hgb from baseline to the final evaluation, was hit, it was just barely statistically significant and at only one dose, with all other doses handily missing (this is also the primary efficacy endpoint in the ongoing phase III CRUISE studies). Again, there was no clear dose-dependent response. Assuming Dr. Yokum's allegations are legitimate, the FDA may have significant concerns about the phase IIb efficacy data. CRUISE studies are relatively long (12 months) and costly which, coupled with potentially questionable phase II efficacy data and allegations of managerial misconduct, introduce what we believe is meaningful risk that shareholder value could end up being impaired.

- **ESA Sparing Not Overly Compelling**
  While the limited data that was released relative to ESA sparing in phase IIb indicated that SFP may have utility in reducing ESA dosage, we would characterize the results as inconclusive given the lack of a dose-dependent response of SFP on ESA dosing. While ESA reduction will not be required for FDA approval, RMTI clearly views it as the major selling point for SFP as it would require the use of less ESA (compared to IV iron) and would therefore offer relief to the margin squeeze providers will experience from bundled reimbursement and the high cost of ESA.

  In addition, SFP, if approved, will directly compete with long-acting erythropoietin receptor activators (CERA) which also have utility in reducing the amount of ESA. Mircera (methoxy PEG-epoetin B), Roche's CERA drug, is FDA approved and is expected to be available in the U.S. in mid-2014 (which we think is likely to be ahead of SFP).

- **Standard of Care Headwind**
  Even with accepting the premise that that the phase IIb primary endpoint would have been met had protocol violations and other potential extenuating circumstances (RE block from too high of an SFP dose) been controlled for, this might only indicate that SFP is more effective than no iron supplementation. The phase III trials' control arm, similar to phase II, are patients receiving no iron supplement which will reveal nothing about SFP's effectiveness compared to IV iron (the current standard of care) in maintaining Hgb or in ESA sparing. While SFP's safety profile looks to be excellent, in general IV iron is relatively safe. And despite certain risks of IV iron, its use in CKD dialysis patients has been rising, partly due to recent studies showing

effectiveness at increasing Hgb levels and reducing required ESA doses. As such, in the absence of compelling ESA sparing data, we think SFP may face significant headwinds against IV iron given the latter's established position and the "we know what to expect from the standard of care" mentality and related risk aversion to novel products common with health care providers.

- **Development / Commercialization Delays**
  There's been a regular pattern of management pushing back commercialization timelines for SFP and, given that enrollment just completed in July, we think it's highly probable that the CRUISE studies will not complete by mid-2013, which was management's most recent guidance prior to the Q3 2012 conference call. On the Q3 call management noted that they now expect completion in August 2013, implying another (albeit slight) delay from mid-2013. Timelines for commercialization of Calcitriol, which was acquired just barely over one year ago, have also already been pushed back. While optimistic projections relative to development and commercialization timelines are common among life sciences companies, regular and ongoing delays are often indicative of future setbacks that end up being costly and damaging shareholder value.

  In early 2010 RMTI had guided towards an SFP launch date in 2013. Management reiterated this 2013 guidance in May 2011. RMTI then guided towards mid-2013 for the CRUISE studies to wrap up and the most recent guidance is for August 2013. However, we think current best-case scenario is that the CRUISE studies complete in the Summer of 2013, an NDA is filed in late-2013 and SFP launches in late 2014. Again, that's a best-case scenario and assumes no delays during the treatment phase of the studies, with data analysis, with the regulatory filing and with an FDA decision and regulatory turn-around (most importantly it assumes SFP is approved). Best-case scenarios often don't happen, however, and we would be surprised if SFP launches by the end of 2014.

  Calcitriol was acquired in July 2011. At that time management guided towards a launch in Q2 2012 and expected the purchase to be accretive in 2012. By late 2011 the launch guidance was pushed back to the second half of 2012. On the Q2 2012 call (August 2012) management again pushed back the expected launch - to Q1 2013. On the Q3 call (November 2012) the launch was again pushed back - to Q2 2013 where it now stands.

- **Lawsuit Contributes Meaningful Risk**
  A wrongful termination lawsuit[7] was filed in early March 2012 by Rockwell's former V.P. of Drug Development and Medical Affairs (Dr. Richard Yocum who was in charge of the SFP development program) which alleges severe misconduct by company leaders including mischaracterizing the SFP phase IIb clinical trial results as "positive" and failing to disclose RMTI's discord with the FDA on the phase III trial design. While the validity of the allegations is currently unknown, it poses significant risk in our opinion (including significant delays to SFP commercialization, handicapped approvability of SFP, handicapped demand for SFP - any of which we think are real possibilities and could negatively impact the stock price) from the accusations being made. Given the severity of the allegations and potential negative outcomes if they are legitimate (particularly that the FDA may not be in agreement with the CRUISE trial designs), we feel it's prudent to make sure investors are aware of the lawsuit and the possibility that this could be a real cause for concern. RMTI's motion to dismiss the lawsuit was denied by the court on June 27th.[8]

  While we are taking no position on the validity of Dr. Yocum's claims, we highlight several allegations made in the lawsuit[8] that, if legitimate, could be of particular concern. These are;
  - Aside from showing an absence of safety issues, the phase IIb study was a failure (Zacks' note: this is in direct contrast to RMTI's February 2010 press release which was titled, "Rockwell Medical Announces Positive Phase IIb Clinical Data")
  - Yocum and other clinical experts warned RMTI's CEO, Robert Chioni that the results of the phase IIb study did not provide adequate efficacy data or dose ranging information to proceed directly to phase III trials
  - Due to the inadequate dose-selection data and lack of confirmation of efficacy in phase II, Yocum urged RMTI to conduct additional phase II studies before proceeding to phase III
  - In early July 2011, FDA indicated agreement with Yocum's assessment, stating "It appears that no dose response pattern was identified among the dose groups for SFP in your completed Phase II study"
  - In early December 2010 FDA sent RMTI a "No Agreement" letter and rejected RMTI's proposed phase III trial design

[7] United States District Court Southern District of California, Case #3:2012cv00568: Richard Yocum, MD vs. Rockwell Medical Technologies, Inc. and DOES 1 through 25

[8] United States District Court Southern District of California, Yocum v. Rockwell Medical Technologies Inc. Case No. 12-CV-568-MMA(MDD). June 27, 2012. Order Denying Motion To Dismiss And For Transfer of Venue. docs.justia.com

- The parties met in February 2011 to discuss the phase III trial design but the FDA maintained numerous substantive points of disagreement with the proposed phase III trial design, with the agency noting "we are concerned that it will not be possible to reach agreement on the specific features of the study design to ensure its acceptability to support the indication are seeking" (Zacks' note: this bullet-point seems to contradict RMTI's October 20, 2010 press release which notes, "We are pleased that our positive dialogue with the FDA led to what we believe to be a robust Phase III program" and "We are very encouraged that the FDA supports our Phase III primary efficacy endpoint…"[9] as well as the company's November 10, 2010 press release where they announced that they had, "Finalized Phase III trial design with FDA"[10])
- Yocum further alleges that the disagreement was not resolved (Zacks' note: if valid, this is of particular concern as the CRUISE findings, no matter how compellingly positive, may not be acceptable by the FDA as support for approvability of SFP. This means the CRUISE studies could be a very costly mistake.)
- Dr. Yocum claims his termination from RMTI (in September 2011) was a result of his "opposition to fraudulent, unlawful, and unethical acts"

- **Optimistic Calcitriol Projections**

  Management's expectations for their Calcitriol (generic injectable vitamin D analogue) product may be highly optimistic. Management believes Calcitriol can generate $50 million in revenue with implied gross margins of ~50% in the first full year on the market (which they think could be 2013 - or maybe now 2014, given the launch delays). RMTI says revenue will be driven by bundled reimbursement causing widespread switching by healthcare providers from higher-priced competing branded products (namely Zemplar and Hectorol) to their lower-cost generic product. While bundling may cause some switching, given the proven efficacy advantages of competing vitamin D analogues (including Zemplar, Hectorol and Sensipar) and the potential that competitors reduce their prices (particularly with the introduction of generic Zemplar by 2014), we think that $50 million (or ~ 14% market share of the ~$350 market for ESRD vitamin D) in the first year on the market is probably highly optimistic. This also assumes that RMTI first gains FDA approval to market Calcitriol - the company has recently noted that they are currently in the process of getting their manufacturing facility approved - although the expected launch has been delayed from initial expectations (cited in July 2011) of early 2012 (with the acquisition also initially expected to be accretive by mid-2012, obviously neither of which happened).

  Something else that brings into question management's expectations for Calcitriol is the relatively meager acquisition price (i.e. - would the (unnamed) seller sell the ANDA this cheap if they, or another company, thought it could claim double-digit market share in year 1?). Notwithstanding the unique advantage RMTI has with being able to leverage their already established customer base and sales/distribution infrastructure to facilitate sales of Calcitriol, it seems that either management's expectations of the product are highly optimistic or they got the deal of the century. Terms of the purchase were not disclosed but based on RMTI's balance sheet and cash flow statement prior to and following the July 2011 acquisition date, the purchase price looks to be immaterial. RMTI paid an additional $550k in Q3 2012 but all-in, the total acquisition price looks to be approximately $700k. While RMTI will incur additional expenses related to getting their manufacturing facility approved by the FDA, those expenses are not expected to be overly significant. Even if we ballpark $2MM (we think it's actually closer to $1MM) in acquisition and regulatory/facility expenses compared to the ~$50 million in revenue (with implied gross margin expectations of ~50%) management says they expect their Calictriol product to generate in the first full year on the market (which they think could be 2013, or maybe 2014), it seems that either RMTI got an absolutely tremendous deal (i.e. - purchase price ~ equal to 2% of first-year sales or 4% of gross profit) or management's expectations may be highly optimistic. While fire sale prices are not unheard of in pharma/biotech, especially in the case of a larger pharma purging legacy and off-patent assets that don't fit with a sales force and marketing heavy business model, an implied 2% of first-year sales purchase price should raise some eyebrows.

- **Base Business May Have Peaked**

  Base business (hemodialysis concentrates) revenue may have peaked in 2010 at $59.6 million. Revenue fell 18% in 2011 and through the first nine months of 2012 was down 1% y-o-y (although Q2 and Q3 were up slightly). The base business is also relatively low margin (12% - 15% gross margins) and has provided only one quarter (Q2 2010) of positive operating income over the last several years (and that was partially due to relatively low R&D expenses in that quarter). While RMTI's newer powdered concentrates are higher margin due to lower shipping costs, bundled reimbursement which has put downward pricing pressure on all dialysis

[9] Rockwell Medical Technologies Inc. Company *Plans to Start Phase III Within 90 Days*. October 20, 2010

[10] Rockwell Medical Technologies Inc. *Rockwell Reports Third Quarter Results*. November 4, 2010

concentrate products, puts a limit on gross margin expansion. We do not believe that RMTI's base business will be able to generate positive operating income or cash flow. As such, any delays in commercializing the pipeline will be magnified on the bottom line and stress the balance sheet.

OUTLOOK / VALUATION / RECOMMENDATION

Given our aforementioned concerns, we feel there is significant risk that Rockwell's revenue remains relatively flat to only slightly positive through 2015. The company's base-business, hemodialysis concentrates, may have already peaked and we expect this to show continued erosion from here on out. We currently model Calcitriol to launch next year but believe management's sales expectations for their vitamin D analogue product may prove to be wildly optimistic. Our model incorporates the assumption that SFP launches in 2015. Our ~$4 million in modeled SFP revenue in 2015 is already risk-adjusted for what we believe to be material aggregate risk encompassing potential for; delays in the clinical trials/data analysis/regulatory filing/FDA turnaround, failure to hit efficacy endpoints, failure to gain FDA approval, less than compelling ESA sparing, and (assuming approved and launched) a strong competitive headwind.

R&D expense is running $8MM - $10MM per quarter and the company is burning about $9 million of cash per quarter. Given the meager margins and top-line erosion of the company's base-business, if this substantial R&D spend does not produce positive ROI in relatively short-order, shareholder value could be significantly impaired. At the current burn rate the cash balance at 9/30/2012 represented about 4 months worth of operating capital. Based on our current model we do not believe RMTI will generate positive net income or cash flow for the foreseeable future and expect that RMTI will need to continue to raise a significant amount of additional operating capital through at least 2017 (and potentially longer) which could be highly dilutive to the existing shareholder base.

RMTI Looks Overvalued Based On DFC and Comparable Valuation …

Based on our DCF model which goes out to year 2022 and uses a 9.3% discount rate (based on CAPM) and 2% terminal growth rate, RTMI is valued at approximately $4.20/share.

Based on a near-term P/S metric (P/E isn't applicable given that we model negative net income through 2018) and using Fresenius (P/S: 1.6x 2012, 1.5x 2013) and DaVita (P/S: 1.2x 2012, 1.1x 2013) as comps, RMTI is valued at between $2.55/share and $3.80/share.

As we feel near-term P/S under-represents the value of RMTI's pipeline, we think DCF provides a better gauge of the company's intrinsic worth and feel $4.00/share is reasonable fair value of RMTI. While the shares are down about 25% since we initiated coverage in September 2012 we feel stock still trades richer than warranted given the various and significant risks. We recommend selling the shares down towards our $4.00 target price. We are maintaining our Underperform rating and $4.00/share price target.

FINANCIAL MODEL

Rockwell Medical Technologies, Inc.

	2011 A	Q1A	Q2A	Q3A	Q4E	2012 E	2013 E	2014 E	2015 E
Hemodialysis Conc. & Supplies	$48,966.2	$12,028.4	$12,124.8	$12,689.3	$11,988.0	$48,830.5	$47,887.0	$46,163.1	$43,485.6
YOY Growth	*-17.8%*	*-9.5%*	*2.7%*	*6.0%*	*0.8%*	*-0.3%*	*-1.9%*	*-3.6%*	*-5.8%*
SFP	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$3,850.0
YOY Growth	-	-	-	-	-	-	-	-	-
Calcitriol	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$700.0	$4,200.0	$8,400.0
YOY Growth	-	-	-	-	-	-	-	*500.0%*	*100.0%*
Total Revenues	$48,966.2	$12,028.4	$12,124.8	$12,689.3	$11,988.0	$48,830.5	$48,587.0	$50,363.1	$55,735.6
YOY Growth	*-17.8%*	*-9.5%*	*2.7%*	*6.0%*	*0.8%*	*-0.3%*	*-0.5%*	*3.7%*	*10.7%*
Cost of Goods Sold	$43,323.3	$10,401.9	$10,406.0	$11,043.4	$10,321.7	$42,173.0	$40,715.9	$40,592.6	$40,352.6
Gross Income	$5,642.9	$1,626.5	$1,718.8	$1,645.9	$1,666.3	$6,657.5	$7,871.1	$9,770.4	$15,383.0
Gross Margin	*11.5%*	*13.5%*	*14.2%*	*13.0%*	*13.9%*	*13.6%*	*16.2%*	*19.4%*	*27.6%*
SG&A	$9,522.3	$2,898.7	$2,824.4	$3,325.4	$3,015.0	$12,063.5	$11,369.4	$11,633.9	$12,373.3
% SG&A	*19.4%*	*24.1%*	*23.3%*	*26.2%*	*25.2%*	*24.7%*	*23.4%*	*23.1%*	*22.2%*
R&D	$17,805.4	$9,405.5	$10,876.4	$16,238.5	$4,550.0	$41,070.4	$28,145.0	$22,447.0	$19,588.0
% R&D	*36.4%*	*78.2%*	*89.7%*	*128.0%*	*38.0%*	*84.1%*	*57.9%*	*44.6%*	*35.1%*
Operating Income	($21,684.8)	($10,677.8)	($11,982.0)	($17,917.9)	($5,898.7)	($46,476.3)	($31,643.3)	($24,310.4)	($16,578.3)
Operating Margin	*-44.3%*	*-88.8%*	*-98.8%*	*-141.2%*	*-49.2%*	*-95.2%*	*-65.1%*	*-48.3%*	*-29.7%*
Pre-Tax Income	($21,442.6)	($10,566.9)	($11,905.3)	($17,875.8)	($5,884.6)	($46,232.6)	($31,803.3)	($24,470.4)	($16,738.3)
Taxes	$2.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Tax Rate	*0.0%*	-	-	-	-	-	-	-	-
Net Income	($21,444.6)	($10,566.9)	($11,905.3)	($17,875.8)	($5,884.6)	($46,232.6)	($31,803.3)	($24,470.4)	($16,738.3)
YOY Growth	*-699.2%*	*262.8%*	*162.3%*	*254.6%*	*-34.3%*	*115.6%*	*-31.2%*	*-23.1%*	*-31.6%*
Net Margin	*-43.8%*	*-87.8%*	*-98.2%*	*-140.9%*	*-49.1%*	*-94.7%*	*-65.5%*	*-48.6%*	*-30.0%*
EPS	($1.21)	($0.54)	($0.58)	($0.84)	($0.27)	($2.23)	($1.17)	($0.74)	($0.48)
YOY Growth	*669.3%*	*223.0%*	*124.2%*	*197.4%*	*-44.7%*	*84.4%*	*-47.3%*	*-36.8%*	*-35.5%*
Diluted Shares O/S	17,775	19,442	20,568	21,299	21,800	20,777	27,100	33,000	35,000

Brian Marckx, CFA

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MANAGEMENT [11]

Robert L. Chioini

Founder, Chairman, Chief Executive Officer and President

Robert L. Chioini, 46, is the Founder, Chairman, Chief Executive Office and President of Rockwell Medical, Inc. Mr. Chioini has served as the Chairman since March 2000, as well as the President and Chief Executive Officer since January 1995. In addition, Mr. Chioini is a Board Member of Medical Mainstreet, an alliance of world-class hospitals, universities, medical device and biopharmaceutical companies creating a global center of innovation in health care, research and development, education and commercialization in the life sciences industry in Oakland County, Michigan. Prior to founding Rockwell, Mr. Chioini served as Regional Sales Manager for Dial Medical of Florida, Inc., from 1993 to 1995, which was then acquired by Gambro HealthCare, Inc. Earlier in his career, Mr. Chioini served in sales, management and marketing capacities with medical manufacturing companies. Mr. Chioini is a graduate of Michigan State University and earned his Bachelor's degree in 1987.

Thomas E. Klema

Vice President, Chief Financial Officer and Secretary

Thomas E. Klema, CPA/MBA, 56, is the Vice President of Finance, Chief Financial Officer and Secretary of Rockwell Medical and has served in that position since January 1999. Prior to joining Rockwell, Mr. Klema served as the Vice President of Finance and Administration for Whistler Corporation. Previously, Mr. Klema held senior management roles at Molson's Diversey subsidiary, which was acquired by Unilever. While at the Molson Companies and Unilever, Mr. Klema served as Vice President of Finance, Administration and Business Development. Mr. Klema earned his Bachelor's Degree in 1976 and his Master of Business Administration Degree in 1977 from Michigan State University.

Ajay Gupta, M.D.

Chief Scientific Officer

Ajay Gupta, 52, is the Chief Scientific Officer and has served in that position since he joined the company in June of 2009. Dr. Gupta has been a member of Rockwell's Scientific Advisory Board since November, 2005. From 2002 to 2009, Dr. Gupta was an Associate Professor of Medicine at UCLA and Charles Drew University Schools of Medicine in Los Angeles; while at UCLA, he has had an active nephrology practice. Dr. Gupta is the inventor of dialysate iron therapy using Soluble Ferric Pyrophosphate (SFP) as well as the inventor of intravenous (IV) iron therapy using slow continuous infusion of SFP. He has filed a number of patents in the areas of drugs, medical devices and diagnostic tests. Dr. Gupta earned his MBBS degree and completed his residency in Internal Medicine from All India Institute of Medical Sciences (AIIMS), New Delhi. In 1990, he completed a Nephrology Clinical/Research Fellowship from Washington University, St. Louis, Missouri. He has served on the faculty at Washington University, St. Louis; State University of New York, Syracuse; University of Alabama, Birmingham and Henry Ford Hospital, Detroit; MI. Dr. Gupta is the founder and Chairman of the Indian Society for Bone and Mineral Research and has completed a clinical fellowship in Nephrology from Wayne State University, Detroit, Michigan and a research fellowship in Nephrology from Washington University, St. Louis, Missouri

Raymond D. Pratt, M.D.

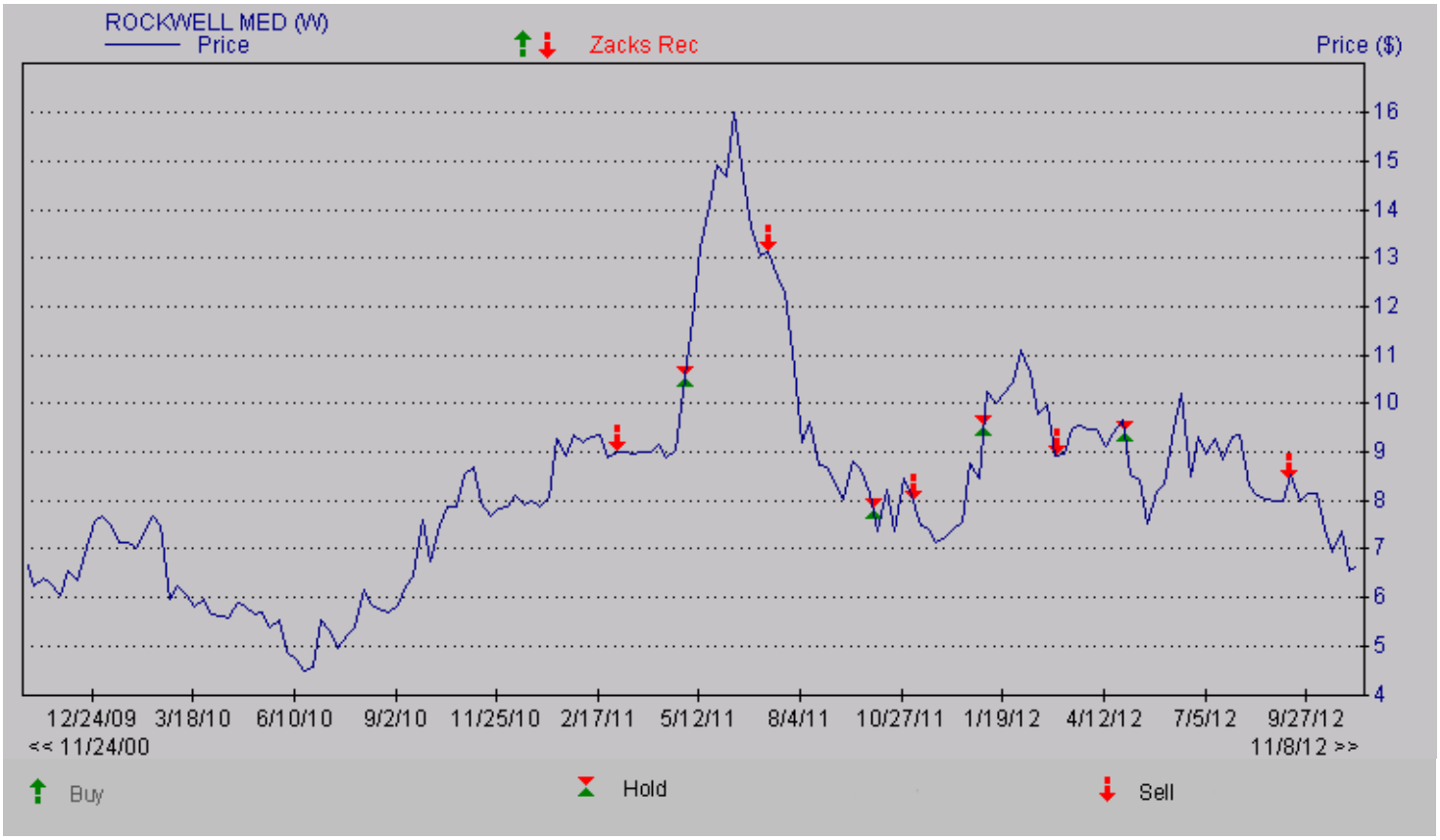
Chief Medical Officer

Raymond D. Pratt, M.D, 60, is the Chief Medical Officer since he joined the company in April, 2012. Dr. Pratt was Vice President R&D and as the scientific leader in its Emerging Business and Renal Business Units at Shire PLLC. Previous roles at Shire included Vice President Global Clinical Medicine and Global Clinical Affairs and head of US Clinical Development. Dr. Pratt was instrumental in the FDA approval of Fosrenol ESRD indication and CKD non-dialysis indication in the European Union and United States. He was responsible for three new drug applications as well as multiple EU applications. He has managed ten different drugs through all stages of global development for renal and other indications and has extensive experience appearing before the FDA. Prior to Shire, Dr. Pratt was Senior Director, Clinical Research and Development at Eisai Medical Research from 1994 to 2003, where he was head of CNS and Internal Medicine clinical development. Dr. Pratt received his M.D. from the University of Illinois College of Medicine. He served six years in the U.S. Army Medical Corps including a period as Director, Dialysis Services at the Walter Reed Army Medical Center. He has served as an Assistant Professor at Cornell Medical College from 1993 to 1994 and at Johns Hopkins University School of Medicine from 1990 to 1993.

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