



RMJ Holdings, LLC

DEVELOPING RMJH-111B:
MAGNESIUM REINVENTED

Caution Regarding Forward-Looking Statements

Forward-looking statements in this information are based on current plans and expectations that are subject to uncertainties and risks. The following factors, among others, could cause our actual results to differ materially: our ability to obtain the capital required for research and operations; the inherent risks in drug development including the progress of our clinical trials and demonstrating efficacy; development time/cost and the regulatory approval process. Forward-looking statements here speak only as of November 25, 2019, and we assume no obligation to update forward-looking statements or the reasons why actual results could differ. This information is not a solicitation or offer to sell securities.

CORPORATE HIGHLIGHTS

- Significant unmet cardiovascular need... 25 million+ initial US market
- Delivery technology provides threefold uptake- "Magnesium reinvented"
- Successful Phase 1 / 2 clinical trial with FDA agreement on roadmap
- Pivotal Phase 3 trial designed for rapid completion and 505(b)(2) approval
- Strong IP with protection through at least 2027 for platform & pipeline
- Opens a new category in hypertension - attractive for value-based payments
- Licensing strategy: Fastest path to monetization
- Seasoned, experienced senior team to execute novel trial design

ESSENTIAL HYPERTENSION: BIG UNMET NEED FOR INNOVATION

- ≈46% (≈100 million) adults in US are hypertensive (by 2017 guidelines)
- Risks from CVD, stroke & heart attack
- ≈25% hypertensive patients treated with diuretics initially and ≈50% eventually
 - Lower BP goals (treat above 130/90)
 - CDC: hypertension top health priority
- Essential Hypertension in US accounts for:
 - ≈14% of all cause mortality [>300,000/yr]
 - ≈ 6% of all disability (2007)

Magnesium rarely used due to poor tolerance of *currently* available forms that lack RMJH-111B's enhanced uptake & engaged retention

RMJH-111B COMMERCIAL OVERVIEW

- **First drug candidate applying patented inverted micellar nanodroplet technology licensed exclusively by RMJ Holdings, LLC with fast to market roadmap.**
- *Initial* target market **25 million people on thiazide-like diuretics.**
 - **Initially** as an adjunct to chronic use *approved* medication, 505(b)(2) path.
 - RMJH-111B **reduces kidney harm** due to magnesium wasting that is exacerbated by *all* classes of approved anti-hypertensive medication. The ‘holy grail’ of blood pressure regulation includes modulating tiniest blood vessels that RMJH-111B restores. Existing anti-hypertensives, by contrast, do not reach the critical tiny arterioles often with adverse effects.
 - Added **indications**, as well as combinations and then as polypills. This doubles the number of **peak sales years**.
 - **Pipeline and platform included**

RMJH-111B ADDITIONAL DRUG INDICATIONS RELATED TO MAGNESIUM NEED IN DIFFERENT CELLS AND ORGANS

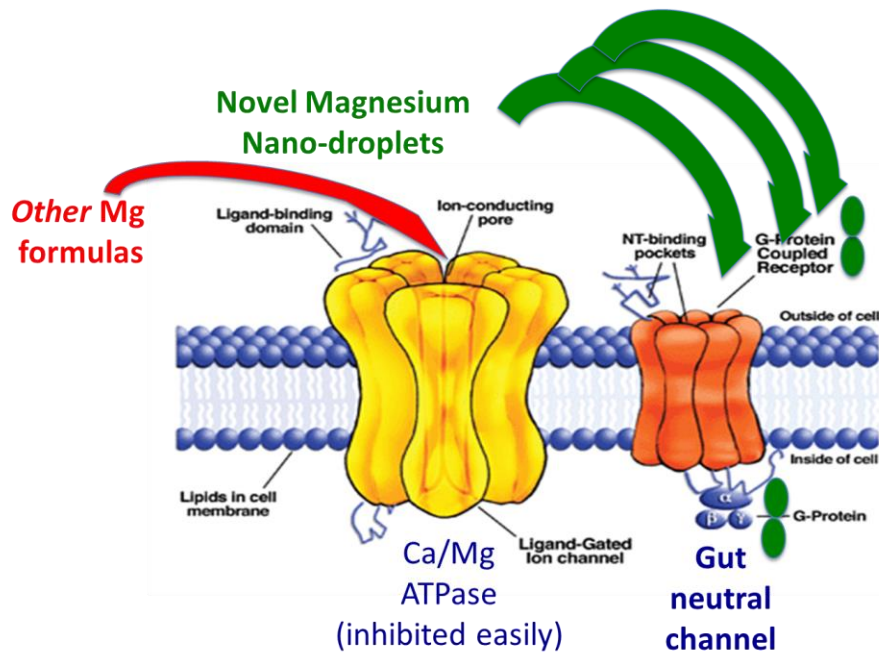
<u>Indications Magnesium Needed</u>	Clinical applications of restoring cell Magnesium
Hypertension	Essential, medication induced
Atrial Fibrillation (A-Fib)	Lack of heart magnesium provokes electrical instability
Myocardial Infarction (Heart Attack)	80+% of MI people have low cell magnesium
Mitral Valve prolapse	Lack of collagen repair of ring that holds the valve
Congestive heart failure (CHF)	Adequate magnesium improves ejection fraction
Atherosclerosis / Stroke	Blood vessels that are repaired function better
Restless legs	Low cell magnesium correlated with twitchy muscles
Fatigue	Low cell magnesium means ATP energy unavailable
Fragile blood vessels	Collagen and elastin impaired repair
Hyperlipidemia	Magnesium protects essential fats in transport
Eclampsia of Pregnancy	Parenteral use, safety of large amounts needed
Platinum chemotherapy	Wastes magnesium; often given IV at each chemo
Diabetes	Metabolic syndrome; Hgb A1c >5%
Migraine headaches	Magnesium relaxes tiny blood vessels in spasm
Osteoporosis	Magnesium lack often a main cause of bone loss
Chronic kidney disease	All forms benefit from restoring cell magnesium
Sickle cell anemia	Cells sickle when acidic; less when magnesium buffers metabolic acids

FROM ADJUNCT TO ALL CARDIOVASCULAR+

- **Initial target market 25 million people on thiazide-like diuretics.**
 - **Starting** as an adjunct to a chronic use approved medication. **Initial indication** allows for more rapid, less risk, less expensive drug approval.
 - **RMJH-111B** cooperates with all categories of anti-hypertensive medications.
 - Business Week, 19 September 2019, p 37-43 confirms carcinogenic residue in generic antihypertensive medications.
 - Additional indications (slide 6), in drug combinations & as polypills.
This *doubles peak sales years*.
- **Successful Phase 1 / 2** study resulted in FDA agreement on...
 - **505(b)2 path** with a single Phase 3 pivotal trial of 1000 finished cases
 - **Pivotal trial** can be completed within one year from first subject enrolled.
- Supplemental **NDAs** are planned for additional indications, special populations and other applications of the core technologies in Phase 4, post market surveillance (slide 17).

RMJH-111B NOVEL DRUG CANDIDATE

Company has exclusive rights to a composition of matter patent (US Patent #8,017,160) to enhance by three fold uptake and chaperone delivery of oral magnesium to cells hungry for this essential mineral. This fundamental technology 'reinvents' magnesium through novel uptake and cell delivery of inverted 'nano-droplets' (see below).



Softgel trade secrets

- Charge-neutral nano-droplets (micelles, **tiny drops**) are formed that are taken up by neutral cell channel pores
- **Enhances** magnesium uptake *even* when the usual calcium/magnesium ATPase uptake ion channel is saturated
- **Stable softgel** with long shelf-life
- **Safety, tolerability & efficacy** data from Phase 1 / 2 clinical outcome trial support company's drug approval roadmap

INTELLECTUAL PROPERTY, ISSUED GLOBALLY

United States Patent Issued #8017160

Claim: Magnesium complex consisting of a magnesium salt; a phosphatide a di-carboxylic acid/or tri- carboxylic acid; and a water and glycerol solution

Canada	Issued	#2535932	United Kingdom	Issued	#1660103GB
Europe	Issued	#1660103	Netherlands	Issued	#1660103NL
Switzerland	Issued	#1660103	Poland	Issued	#1660103PL
Czech Republic	Issued	#1660103CZ	Sweden	Issued	#1660103SE
Germany	Issued	#602004053583.0	Hong Kong	Issued	#1089975
Denmark	Issued	#1660103DK	Mexico	Issued	#292147
France	Issued	#1660103FR	Australia & Singapore	Issued Issued	#2011201073

PHASE 1 / 2 TRIAL RESULTS

- Initial study (N=15 on active; 6 on placebo) confirmed strong trend with correlation between improvement in serum magnesium and blood pressure reduction.
- No adverse events; well tolerated
- Benefits observed across the active group
- On analysis, statistical significance would have been achieved if 80-100 people had been studied
- Sufficient evidence for FDA to agree no further phase 2 information needed and a single phase 3 trial sufficient for new drug approval (NDA)

RMJH-111B PHASE 1 / 2 STUDY CONCLUSIONS

Substantial blood pressure improvements over a short treatment period along with the demonstrated safety and tolerability plus other documentation satisfied FDA that Phase 2 is complete. The *initial* indication is as an adjunct to an approved chronic use medication where better outcomes and lower risks are anticipated and documented in the final, pivotal Phase 3 trial. Forward plans include supplemental new drug applications for essential hypertension (eHBP) and other cardiovascular indications during post market surveillance (Phase 4). A pipeline of other drug indications / disease states will be pursued as resources permit (Slide 6).

PHASE 3 PIVOTAL STUDY DESIGN

- Parallel, double-blind study, N=1,000 finished cases (1050 enrolled)
 - 3:1 randomization, 750 on RMJH-111b + 250 on placebo
 - 10 weeks double blind treatment
 - 10 weeks open-label extension
 - 8 weeks randomized withdrawal of responders
 - 42 weeks to exit trial
- **Clinic sSBP** as primary end point; other objectives to address clinical, payor, and consumer needs
- **Serum magnesium** confirms need, efficacy and safety
- Enhanced **arteriolar Magnesium** helps *both* **BP & kidneys**

PHASE 3 PIVOTAL STUDY DESIGN (DERISKED)

- **Clinical risk minimized even with substantial increase in number of participants**
 - **Careful planning and design to address all aspects needed for drug approval.**
 - **Design and strategy supported by minutes of the end of Phase 1 / 2 meeting with FDA.**
 - **WCT (Worldwide Clinical Trials under Dr Neal Cutler) will serve as CRO with trial commencing early in the 2nd quarter 2020.**
 - **RMJ's team includes members who have success with other hypertension drugs obtaining FDA drug approval.**
 - **Other members of RMJ's team edit the guidelines for hypertension clinical management.**
- **The most recent guidelines for high blood pressure urge comprehensive treatment earlier, starting now at 120/80 rather than 130/90.**

PHASE 3 PIVOTAL STUDY DESIGN (DERISKED)

- Retrospective analysis of the data from the Phase 1 / 2 study showed strong favorable trends and correlations such that <0.05 p value (significance appropriate for approval) would have been achieved if only 80 additional subjects had been included.
- Statistical design for the Phase 3 trial includes 300 additional patients which will result in the study being overpowered to achieve significance in a 'once and done' approach to drug approval. The initial 300 participants to complete the protocol will then be re-randomized to assess adaptation (technically tachyphylaxis) over an additional eight weeks. Participants will return two weeks after completing the study for safety and final assessments. This step is critical for approval and including it in this trial will ensure a once and done and save substantial dollars and a year's time.
- FDA agrees that RMJ has built a 505(b)(2) bridge to the approved parenteral magnesium suitable for the oral indication.
- Strategically, more than 80 percent of the trial costs are up front thus overpowering the study with additional patients lowers the total cost and dramatically shortens the time to drug approval by at least a year.

RMJH-111B STATUS

- Fundamental, proprietary advance in magnesium uptake and retention
- 1st in and out of clinic for new drug category; Phase 2 complete
- Single dose, single study sufficient for 505(b)2 NDA
- Phase 3 design: 'Once and done'
 - Quality cases rapidly enrolled, analyzed and reported
- Chemistry, clinical, non-clinical, statistics & toxicology clarified with Cardio-Renal division of FDA

FDA DRUG APPROVAL REQUIREMENTS

Company's Phase 3 protocol and roadmap includes agency's guidance regarding what is required to de-risk the five key areas for drug approval.

Chemistry / CMC: Validated methods (stress tested), GMP, GLP ✓

Clinical (Phase 3 trial; 505(b)2 path) ✓

Safety, tolerability, efficacy, adaptation, and anticipatory assessments

Non-clinical: Literature, global, in FDA preferred format ✓

Statistics: Designed to achieve 0.00125 significance; over powered ✓

Toxicology: Nothing additional needed ✓

RMJH-111B PLATFORM AND PIPELINE, EACH WITH DISTINCT LOOK, FEEL, DOSAGE AND FORM

Cardiovascular drug Platform:

- Essential hypertension starting with thiazides [Rx sooner & easier]
- Better blood lipids
- Atrial Fibrillation
- Congestive Heart Failure (CHF)

Follow-on Pipeline of Indications

- Preeclampsia and eclampsia of pregnancy
- Muscle cramps, restless legs, facial ticks & twitches
- Diabetes, metabolic syndrome & insulin resistance
- Kidney disease
- Osteopenia / Osteoporosis
- Migraine headache
- Sickle Cell Anemia (Orphan Drug candidate)
- Platinum Chemotherapy (cis-platinum *et al...*)

Inadequate hypertension control in people on diuretics is 1st indication for faster drug approval.

HYPERTENSION... HOW LOW TO GO?



American Heart Association, American College of Cardiology and 9+ other health professional organizations released comprehensive new high blood pressure guidelines (11/17).

“Normal BP” *now* <120/80 mm Hg.

Under new guidelines **nearly half of the U.S. adult population (46%) has high blood pressure**, rather than 1 in 3 U.S. adults (32%) with the prior definition.

**High blood pressure redefined for first time in 14 years:
Above 120 is the new treatment consensus guideline.**

ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines, Hypertension. 2018;71:e13-e115, originally published November 13, 2017



RMJ Holdings, LLC

**BIG UNMET CLINICAL NEED FOR SAFER
HYPERTENSION MANAGEMENT**

HYPERTENSION RIPE FOR INNOVATION

HYPERTENSION TRENDS

Near term to best of RMJH Rx knowledge

- No new medications
- No new interventions
- No new procedures

Favorable Market Dynamics (US & Global):

- Payor trends toward **value**-based payment
- Updated **definition** of hypertension
- Cost/benefit analysis

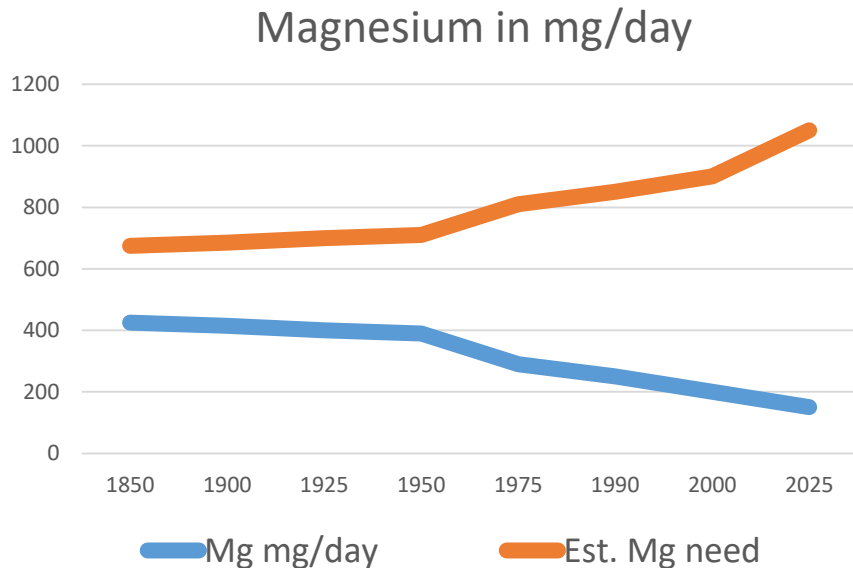
MAGNESIUM MARKETPLACE 2010-2020

150 MM US adults deficient in Mg; relates to *most chronic illness, particularly heart, blood vessels, brain and organ dysfunction*

- Ron Elin's Chronic Latent Magnesium Deficiency (CLMD); confirmed; consistent with 2017 hypertension guidelines
- Bridge from IV to oral agreed by FDA
- Eclampsia & platinum chemo (100,000 US adults annually)
- \$4 Billion US *parenteral* market, (2011), Fresenius Kabi® & Pfizer®

GROWING MG NEED, SAFETY, & EFFICACY FROM RMJH-111B: DIET INSUFFICIENT & CELL LEVEL DECLINING

Daily Ingestion Vs Need



Magnesium is...

- Nature's calcium channel blocker;
- Required to activate many enzymes;
- Protective of essential fats in transit;
- Needed to activate ATP for cell energy;
- Needed for mitochondrial proton gradient.

Less today in soil/diet (US & Global)

60-70+% US & Brazil have confirmed inadequate daily intake of Mg results in chronic latent **magnesium deficiency, being *in lower half of serum Mg lab test range.***

DRI (adults): 310-400 mg/d

Piovesan D *et al*, BMC Bioinformatics, 2012; 13(S14): S10

Sales *et al*. Nutricion Hospitalaria, 2014; 30(1): 200-204

Nielsen FH. Nutrition Rev, 2010; 68: 333-340

[Elin RJ](#), Re-evaluation of the concept of chronic, latent, magnesium deficiency. [Magnes Res.](#) 2011 Dec;24(4):225-227. doi: 10.1684/mrh.2011.0298

HYPERTENSION MARKET OPPORTUNITY

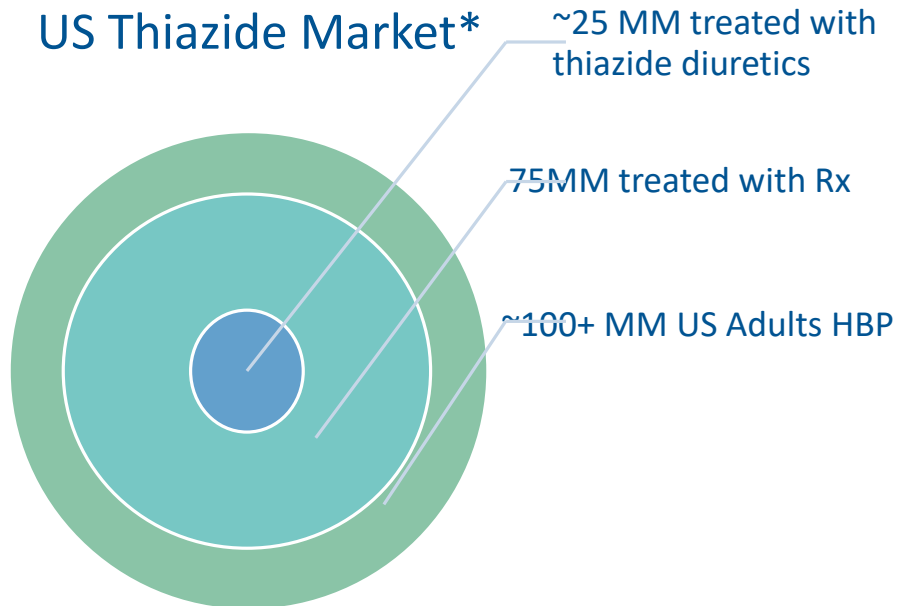
Global push to treat essential high blood pressure (eHBP) earlier, with safer, effective drugs to reduce adverse effects from existing therapies.

HBP MARKET GROWING 1.5%/YEAR	RMJH-111B INITIAL INDICATION	HBP RX SALES, ANNUAL
<p>≈ \$40+ Billion US, 100+ MM eHBP people</p> <p>≈ \$60+ Billion ex-US, 200 MM eHBP people</p>	<p>≈ 20% diuretics <i>first treatment</i></p> <p>≈ 28% of all people with eHBP</p> <p>≈ 50% combo diuretics + others</p> <p>≈ 50% take Rx as prescribed</p> <p>Mg replenishment improves outcomes; reduces side-effects</p>	<p>≈ \$ 5 Billion US diuretics only</p> <p>\$7.5 Billion Ex-US</p> <p>≈ \$10 Billion US for combo diuretic therapy</p> <p>≈ \$15 Billion Ex-US for combo diuretic therapy</p>

<https://www.prnewswire.com/news-releases/global-hypertension-drugs-market-2016-2020---growing-older-population--patent-expiries-of-major-drugs--increase-in-awareness---research-and-markets-577465241.html>
http://www.who.int/gho/ncd/risk_factors/blood_pressure_prevalence_text/en/

MARKET VALUE AND PROJECTIONS

Internal projections, based on an anticipated 15% share of thiazide market plus minimal (~1%) off-label monotherapy use, put peak year sales for *this* indication at \$1.9 Bn.



PEAK YEAR SALES PROJECTION

Based on low price/high market share strategy; 10% royalty

Annual cost of RMJH-111B =
\$540 x ~3.75 million treated

= ~\$1.9 Billion annual
(Projected royalty revenue =
\$190 Million US annually)

*Trends in Antihypertensive Medication Use and Blood Pressure Control Among United States Adults With Hypertension, Qiuping Gu, Vicki L. Burt, Charles F. Dillon, Sarah Yoon, *Circulation*. 2012;126:2105-2114, originally published October 22, 2012



RMJ Holdings, LLC

RMJ HOLDINGS AND RMJH-111B

ABOUT US

RMJ HOLDINGS, LLC, MANAGEMENT

Russell M. Jaffe MD, Ph.D., CCN, Founder and Chief Executive Officer

Dr. Jaffe, an internal medicine physician, clinical pathologist, immunologist, and biochemist, founded RMJH after identifying a need for enhanced uptake and chaperoned delivery of essential minerals, the first of which is Magnesium. He is a Diplomate of the National Board of Medical Examiners and the American Board of Pathology for Clinical and Chemical Pathology. He founded **ELISA/ACT**® Biotechnologies (EAB) the exclusive provider of the lymphocyte response assay (**LRA by ELISA/ACT**) tests – the gold standard in delayed hypersensitivity testing. He also founded **PERQUE**® which develops and sells a new generation of nutritional supplements, available only through doctors and healthcare professionals which have the advanced, mostly proprietary formulas to provide superior, safer results in restoring, maintaining, and enhancing health.

David H. Fater, Executive Vice President

David Fater has extensive experience as a Chief Executive Officer with drug discovery companies focused on stroke and traumatic brain injury as well as a medical device company focused on cardiology. He has also been the Chief Financial Officer for three healthcare companies in which he led the Initial Public Offering. Prior to his corporate experience, he was an international partner with Ernst & Young.

Mischelle Hall, Chief Operating Officer

Mischelle Hall has 20 years of pharmaceutical and nutraceutical marketing and operations experience. She has led Marketing for several organizations focused on multiple categories including hypertension, antidepressants, and women's health. Mischelle earned an MBA from Georgia State University.

Diana Wardak, Chief Financial Officer

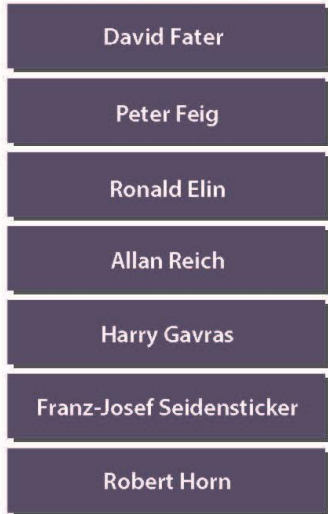
Diana Wardak is a CPA with over 15 years of experience helping organizations in different industries achieve success in revenue growth, compliance and audits. She has both a BA (Law and Political Science) and a BS (Accounting) from Strayer University.

ADVISORY BOARD / CLINICAL STUDY LEADERS

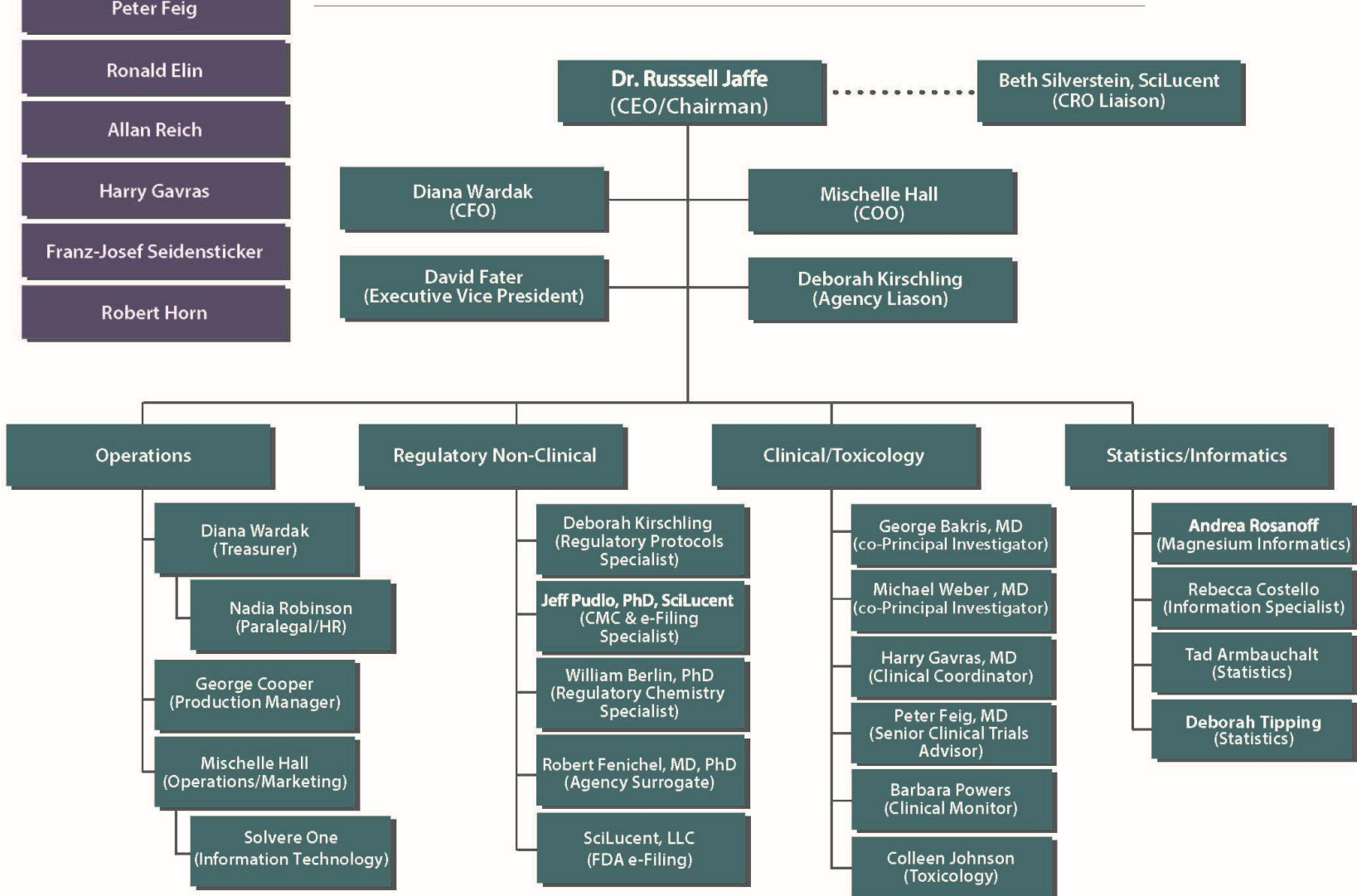
- Ronald Elin: <https://louisville.edu/medicine/departments/pathology/faculty/elin>
- Peter Feig: <https://biography.omicsonline.org/united-states-of-america/sarfez-pharmaceuticals/peter-feig-160736>
- Harry Gavras: <https://www.bumc.bu.edu/busm/profile/haralambos-gavras/>
- Alan Reich: <https://www.seyfarth.com/AllanReich>
- Franz-Joseph Seidensticker:
<https://www.bain.com/our-team/franz-josef-seidensticker/>
- Robert Horn: <https://www.huschblackwell.com/professionals/robert-horn>
- George Bakris: <https://www.uchicagomedicine.org/find-a-physician/physician/george-bakris>
- Michael Weber: <https://www.cardiometabolichealth.org/michael-weber.html>

RMJ Holdings

Advisory Board



RMJ Holdings, LLC Organization Chart



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