RMJ Holdings, LLC

RMJH-111B Opens a new category of drugs to treat essential hypertension: RMJH-111B meets big unmet need

Global patents on novel technology provide the ability to chaperone and deliver this magnesium-based drug to where it can be the most efficacious.

RMJH-111B is an advanced new drug candidate with a full approval roadmap developed by RMJ Holdings, LLC (RMJH). This background document addresses:
1) Description of the novel softgel used in the successful Phase 1 / 2 clinical trial to chaperone and target the delivery of the drug for maximum effectiveness as well as the results of the trial,
2) Need for RMJH-111B beyond hypertension,
3) Phase 3 pivotal trial plan to ensure a rapid study completion followed by New Drug Approval, and,
4) Roadmap to approval and monetization.

1) A **novel drug**, RMJH-111B…

- … is based on patents that cover Dr. Jaffe's invention exclusively licensed to RMJH, royalty-free.
- … enables the magnesium-based drug to be delivered in conjunction with a safer, novel, softgel with a long shelf life stability developed through a reliable and significant drug development partner (Patheon, part of the Thermo Scientific family).
- … has demonstrated enhanced uptake of the magnesium-based drug without the unpleasant side effects compared to any other magnesium oral preparation in an indicative Phase 1 / 2 clinical study.
- … shows promise to provide significantly better outcomes in cardiovascular health and in chronic disease management at lower net risks and costs.

RMJH's proprietary inverted micellar technology has received a **fundamental, composition-of-matter patent enabling** (patent # 8,017,160, issued 09/2011) **the drug novelty and delivery mechanism to be viewed as a new drug (and patented as such), yet it qualifies for 505(b)(2) accelerated drug approval from a regulatory perspective, thereby accelerating New Drug Approval at a substantial reduction in cost.**

- The globally patented inverted micellar nanodroplets enhance the uptake and cell retention of the magnesium by design. This provides the first fundamental enhancement of magnesium uptake and retention in decades. The result reinvents magnesium and **distinguishes it from the many over-the-counter magnesium preparations that all depend upon ion channel uptake and delivery.**
- RMJH-111B's tiny nanodroplets are neutral on the outside with all positive and negative charges balanced in a stable emulsion that can be easily and fully taken up by neutral cell pores and then delivered to cells' interior. **This is in contrast to the ion channel that usually takes up calcium and magnesium that has, at best, one third (33%) uptake of the dose given so our technology enables much more absorption thus increasing efficaciousness.**
- Most magnesium taken orally is retained in the intestines and easily induces hypermotility and diarrhea, preventing any meaningful benefit, limiting dose and patient adherence. Real world

evidence has also demonstrated that magnesium in RMJH's unique form lowers blood pressure when combined with existing high blood pressure medications.

A successful Phase 1 / 2 trial of RMJH-111B demonstrated substantial lowering of blood pressure safely and effectively without the side effects commonly associated with higher oral magnesium intake.

- RMJH-111B demonstrated as much blood pressure reduction in one week as would be expected in 12 weeks based on the hypertension literature. In addition, safety, tolerability and efficacy were demonstrated across the study population.
- Data from the Phase 1 / 2 study showed strong favorable trends. Retrospective calculations showed that $p<0.05$ significance (appropriate for drug approval) would have been achieved if as few as 100 subjects had been studied.
- By including 250 extra patients in the planned pivotal 1,000 patient Phase 3 trial, RMJH's strategic statistics team led by Tad Armbachault are confident the study is overpowered to achieve superior statistical significance in a 'once and done' drug approval approach.
- Magnesium is water soluble; it is regulated by the kidneys. Excess magnesium does not occur in people with reasonable kidney function, even when large doses are taken. RMJH has reviewed the world literature on magnesium and health and is confident that its demonstrated safety and tolerability in the Phase 1 / 2 study has also been confirmed through real world experience. RMJH's global review of relevant literature confirms RMJH-111B's planned roadmap.

2) **Magnesium need** today is greater by more than half than in prior decades due to the sum of stress, toxins and dietary depletion of this essential mineral. Blood pressure medicines commonly deplete cell magnesium.

- Chronic latent magnesium deficiency (CLMD) was initially defined by Ron Elin who is one of RMJH's pioneer investors and is an RMJH advisory board member. Drs. Elin and Jaffe trained together at the NIH Clinical Center in the 1970s.
- CLMD is defined as having a serum magnesium level in the lower half of the serum magnesium range. Magnesium *cell* sufficiency is defined as having a serum magnesium level in the upper half of the serum magnesium range.
- CLMD has been validated by multiple studies over the last decade. This means an inexpensive, generally available blood test is available that will confirm medication need, benefit and safety.

3) The Cardio-Renal section of the FDA oversees RMJH-111B's **drug approval** process. RMJH is ready to conduct a Phase 3 clinical trial, the parameters of which have been reviewed by advisors to the FDA as part of RMJH's full drug approval roadmap.

- End of Phase 2 (type B) meeting minutes are available as part of confidential discussions.
- The same formulation is planned for the final trial with validated and stress tested methods to satisfy FDA and EU requirements for full drug approval.

- The initial indication for drug approval is as an adjunct to thiazide-like diuretics. The 505(b)(2) pathway for oral RMJH-111B includes a bridge to prior approved IV preparations of magnesium as reference. This allows for a single final study that adequately addresses safety, tolerability, efficacy and adaptation. Drug approval as an adjunct to an approved chronic use medicine can be achieved years sooner with fewer subjects and substantially reduced costs. RMJH has prepared a special protocol amendment (SPA) for submission that confirms all that is required to further validate the company's drug approval roadmap.

- An elegantly simple design for a single final Phase 3 trial has been well vetted by outstanding master clinical research organizations including Worldwide Clinical Trials (WCT).
    - WCT is confident that with sufficient funding, this study can be in clinic by early second quarter 2020 and out of clinic by end of the year. This is based on a combination of technology and experience to rapidly enroll quality cases and to reach significant end point results along with all critical assessments for each of the stakeholder groups needed to successfully market a new cardiovascular medicine.
    - RMJH-111B's knowledge network includes a full range of thought leaders in cardiovascular medicine. The study leadership team includes those who have introduced all of the existing categories of hypertension medicines.
        - Principal investigators George Bakris, MD and Michael Weber, MD, are hypertension thought leaders, along with a full team of cardiovascular drug approval specialists.
- Other key points about the pivotal study include:
    - RMJH's strategic and tactical planning shortens the time from study completion to NDA submission by at least six months.
    - Data collected will be verified in real time. This improves data audit quality while reducing time and costs to externally validate data collected.
    - Other than safety specimens, a central lab will receive and archive specimens to be analyzed during the final phase of the study. This reduces costs and improves data quality.
    - RMJH's FDA liaison/regulatory affairs person did a commendable job in the clinical study report submitted and accepted by the FDA. She coordinates all regulatory NDA reporting to include chemistry, clinical, non-clinical literature, toxicology and statistics and it is anticipated that she will do and coordinate the same for the pivotal study.

4) In regard to currently approved high blood pressure medicines, calcium channel blockers and diuretics are known to deplete cell magnesium while sub-optimally reducing blood pressure. Indeed, all of the currently approved high blood pressure medicines will benefit when RMJH-111B is generally available.

- Cooperating rather than competing with other approved hypertension medications reduces their risk by combining several medicines to achieve synergistic benefits. Polypills are anticipated. Taken together this sequence doubles the projected peak sales years and enhances the addressable market.

- What calcium activates, magnesium calms. An increasing number of people (50% of the population) are chronically deficient and low cell magnesium imposes health risks. Magnesium is required for many cell functions and renewal of cellular structure.

We believe RMJH would be attractive to a tactical alliance partner based on the initial drug approval to be followed by an out-licensing strategy. Subsequent additional increases in value would be achieved as the full cardiovascular platform and chronic disease pipeline indications are approved through supplemental and abbreviated NDAs .

After hypertension, there are multiple health conditions that benefit from a magnesium-based drug that uniquely delivers the mineral to cells with fewer side effects. A data package is available upon request.

- Based on documented chronic latent magnesium deficiency (CLMD). each of the potential cardiovascular pipeline and chronic disease platform drug indications address tremendous unmet needs.
- Having a generally available inexpensive blood test that confirms need, efficacy after taking the medication, and safety is important to achieve new drug approval.
- An active petition is underway to substantially increase the Daily Value (DV) for magnesium.

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Caution Regarding Forward-Looking Statements

Forward-looking statements in this document 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 in this document speak only as of the date of the document, and we assume no obligation to update forward-looking statements or the reasons why actual results could differ. This docum is not a solicitation or offer to sell securities.