DEVELOPING RMJH-111B:
A NEW CATEGORY OF CARDIOVASCULAR DRUGS

COMPELLING NOVEL NEW DRUG… NEED, NOVELTY, EVIDENCE, ROADMAP

- Big unmet need for safer, effective blood pressure Rx
- 25+ million initial candidates (US)
- Novel technology provides threefold enhanced active agent bioavailability
- Strong global issued IP with protection for platform and pipeline
- New hypertension category allows for value-based payor negotiation
- Successful Phase 1 / 2 trial with FDA agreement on new drug approval roadmap
- Pivotal Phase 3 trial designed for rapid completion and expedited approval

RMJH-111B UNIQUE OPPORTUNITY

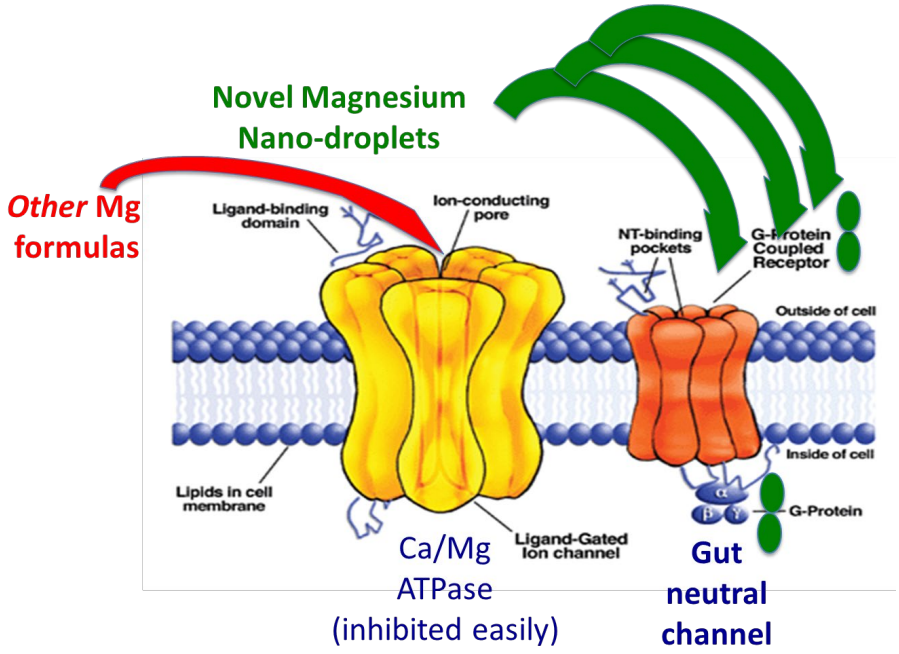
- 1st drug candidate applying globally patented inverted micellar nanodroplet technology to enhance bioavailability and benefits
- *Initial* target market 25+ million people on thiazide-like diuretics.
  - Initially… as adjunct to chronic use *approved* medication (sooner and easier initial approval).
  - RMJH-111B helps open tiniest blood vessels that existing anti-hypertensives do not reach.
  - Multiple drug indications, multi-medication combos and polypills. This *doubles* the peak sales years.
  - Pipeline and platform of additional drug indications included.

FROM ADJUNCT TO ALL CARDIOVASCULAR+

- Successful Phase 1 / 2 study resulted in FDA agreement on…
  - Single Phase 3 pivotal trial of 1,000 completed cases.
  - Pivotal trial can be completed within one year from first subject enrolled.
  - Expedited drug approval using 505(b)(2) pathway.
- Supplemental drug approvals are planned for:
  - Additional indications,
  - Special populations and
  - Other applications of the core technologies in Phase 4, post market surveillance.

RMJH-111B 'REINVENTS' MAGNESIUM

Company has exclusive rights to 'nano-droplet' technology through composition of matter patent (US Patent #8,017,160). Claims include enhanced uptake and chaperoned delivery of oral magnesium to cells hungry for this essential mineral.



Softgel novel trade secrets

- Charge-neutral stable nano-droplets (micelles, tiny drops) are formed 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 approval roadmap

http://en.wikipedia.org/wiki/Endomembrane_system

PHASE 1 / 2 TRIAL RESULTS AND CONCLUSIONS

- Initial study 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 post study analysis, statistical significance (necessary for New Drug Approval) would have been achieved if just 100 people had been studied
- FDA agrees that Phase 2 is complete and clinical study report is sufficient to proceed to a single Phase 3 trial addressing all requirements for new drug approval (NDA)
- Forward plans include supplemental new drug applications for essential high blood pressure (eHBP) and other cardiovascular indications during Phase 4 (post market surveillance).

PHASE 3 PIVOTAL STUDY DESIGN

- Parallel, double-blind study, N=1,000 finished cases
  - 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; 5% sample for 24° blood pressure measurement
- Clinic seated systolic and diastolic pressure as primary end points; other objectives to address clinical, payor, and consumer needs
- *Serum* magnesium is a generally available, inexpensive test to confirm need, efficacy and safety
- Enhanced arteriolar magnesium helps *both* healthier BP & kidneys

PHASE 3 PIVOTAL STUDY DESIGN (DE-RISKED)

- Clinical risk minimized with substantial increase in number of participants warranted by literature and Real-World Experience with magnesium
  - Careful planning and design addresses all aspects needed for NDA.
  - Strategic design supported by end of Phase 1 / 2 FDA meeting minutes.
  - WCT (Worldwide Clinical Trials under Dr Neal Cutler) will serve as CRO with trial designed to commence within 3-4 months of funding.
  - RMJH's team includes members who pioneered other hypertension drugs such as beta-blockers and ACE inhibitors.
  - Other members of RMJH's team edit the hypertension clinical management guidelines used to guide payors and policy experts.
- The most recent guidelines (2017) call for earlier treatment of high blood pressure starting now at 120/80 rather than 130/90.

DE-RISKED PHASE 3 STUDY AND NDA ROADMAP

- Statistical design for the trial includes 300 additional patients
  - Study overpowered by design to achieve 'once and done' drug approval.
  - The initial 300 participants to complete the full protocol will be re-randomized to assess adaptation (technically tachyphylaxis) over an additional eight weeks.
  - Participants will return two weeks after completing the trial for safety and final assessments. This once and done design reduces costs and time.
- FDA agrees that RMJH has built a 505(b)(2) bridge to the approved IV magnesium for this innovative, oral administration.
- 1st in and out of clinic to become first new drug hypertension category in 30+ years

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)

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

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…)*

ADVISORY BOARD / CLINICAL STUDY REGULATORY LEADERS

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