Industry
Biological Device

Key Features
ARLP, LLC is developing first-in-class disruptive technology that will replace electronic pacemakers. The cumulative market size exceeds $4 billion. Company's intellectual property will provide protection through 2021 but new composition of matter application will be filed before initiation of clinical trials. Research and development to date benefited from $24 million in funding. ARLP, LLC plans to file an IND within two years from funding and exit upon initiation of Phase I/ II trials within five years. ARLP identified partners who will produce GMP-grade devices and donate catheters for development. Because initial clinical trial will focus on administration of ARLPs as tandem therapy for treatment of bradycardia the combined Phase I/II study is expected to enroll 10 patients for 12-month study.

Company Resources
License Agreement between Columbia and ARLP, LLC will be executed upon funding.

Pre-Money Valuation:
$4,000,000

Financing Sought:
$7,000,000

Total External Capital Invested
The laboratories of Drs. Rosen and Cohen have been consecutively funded by the NIH for the past two decades with cumulative funding approaching $24,000,000, in direct costs.

Awards/Recognition
Among the awards conferred on Dr. Rosen are: American Heart Association Award of Merit; American Heart Association Chairman's Award; American

Business Description: Autonomically-Responsive Leadless Pacemakers Limited Liability Corporation (ARLP, LLC) is a virtual spin off from Columbia University focusing on late pre-clinical and early clinical development of a new class of pacemakers for treatment of arrhythmias addressing $4 billion global market. This technology is a biological pacemaker that assists in the depolarization and subsequent action potentials required for a proper heartbeat. It utilizes adenoviral vectors to deliver ion channel genes into heart tissue, resulting in the overexpression of these ion channels, and correction of the beating rate of individuals with arrhythmia. Immunocompatibility is high since this invention does not involve implantation.

Present electronic pacemakers are subject to lead fractures, battery replacement, infections, interference from other electromagnetic devices, do not respond to emotions and do not deliver optimal cardiac output. ARLPs overcome all of these clinical shortcomings. Development of the ARLP benefited from $10 million research support and another $14 million in grant support from the NIH. Columbia patented the composition of matter and its utility with last patent expiring in 2021 but new patent application protecting the clinical candidate will be filed before initiation of clinical trials. ARLP, LLC is ready to initiate long-term canine studies with GMP-grade material in support of IND filing within two years from funding. Cost of development through initiation of Phase I/II clinical trials is expected to approach $7 million.

ARLPs are expected to be rapidly adopted by cardiologists because we will initially administer ARLPs to patients with functional electronic pacemakers but partially depleted batteries to extend the battery energy for life and to make the pacemaker autonomically responsive. Once safety is firmly established there will no longer be need for tandem administration and ARLPs would be expected to take over electronic pacemakers. We anticipate selling ARLP, LLC or executing a co-development agreement with biotech or pacemaker manufacturer within 5 years from funding. The Company's value at that time should exceed $70 million, thus providing investors with 10x ROI.

Market size and growth: The current global cardiac pacemaker market is about $4 billion and expected to grow at CAGR of 11% during the next 6 years. US market accounts for nearly 40% of the total market and Europe accounting for about 30%. Asia Pacific market is growing at 13.3% CAGR[1]. The concept of ARLPs could be leveraged to develop pacemakers for other medical indications such as:

- Atrio-ventricular node
- Gastric pacemaker to signal satiety
- Laryngeal muscle stimulation
- Hyperirritable bladder control
- Chronic pain treatment
- Refractory hypertension treatment

[1]Transparency Market Research

Scientific Expertise: ARLPs are devices incorporating three areas of scientific expertise

- electrophysiology
- transfection technology
- cardiology

Opinion makers in these fields, Michael Rosen from Columbia University and Ira Cohen from Stony Brook University contributed their knowhow to create this innovative product. The complexity of the technology presents a significant technological hurdle for competition. Our scientists are opinion leaders in the field.

Technology: Our research suggests that biological pacemakers can perform superior to implantable, electronic pacemakers in producing a physiological heart rate, making them useful in treating a number of cardiac arrhythmias. Adenoviral delivery assure biological pacemaker robustness and longevity due to administration to post-mitotic cells. Current clinical trials with unrelated treatments using adenoivirus suggest that adenoviral delivery could be used as the optimal method of introducing gene therapies into patients.

Overexpressing different combinations of ion channels in cardiac tissue can produce varying results that could be useful in tweaking biological pacemakers to suit individual needs.

Heart Association Distinguished Achievement Award; Leiden University Einthoven Award; Heart Rhythm Society Distinguished Scientist Award; Cardiac Electrophysiology Society Gordon K. Moe Lectureship and Russian Academy of Sciences Doctorate Honoris Causa;

Scientific Advisors

Michael R. Rosen, M.D.
Gustavus A. Pfeiffer Professor of Pharmacology, Professor of Pediatrics, Director of Center for Molecular Therapeutics, College of Physicians and Surgeons of Columbia University

Ira Cohen. M.D., Ph.D.
Leading Professor of Physiology and Biophysics, Director of Institute of Molecular Cardiology, Stony Brook University

Corporate Management

CEO: ***Annemarie B. Moseley, M.D., Ph.D.***
Chairman, CEO and Founder of REPAIR Technologies, Cognate Therapeutics and Osiris Therapeutics, Executive consultant, Compass Venture Group/Abbot BD

Chief Clinical Officer: Warren Sherman, M.D.
Chief Medical Officer LoneStar Heart, Inc., Clinical Advisor, Past Chief Medical Officer Celyad S.A.

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Intellectual Property: Columbia's existing issued patent is expected to provide protection through 2021 but Columbia intends to file new patent application, protecting the final composition of matter, before we initiate clinical trials.

Regulatory Strategy: Our regulatory strategy is guided by the need for a safe and autonomically-responsive therapy that eliminates the need for periodic replacement of batteries, replacement of fractured leads or short leads in pediatric patients as they grow and that avoids potential infections of hardware directly in touch with blood. Such a therapy would be initially co-administered along with electronic pacemakers to induce rapid adoption by risk-averse cardiologists and to provide appropriate safeguards in clinical trials. The shortest and least expensive clinical trial would involve administering the ARLPs to avert power pack replacement. This should be more acceptable to the Institutional Review Board, FDA, the interventional cardiologists and to the patients because the patients would continue benefiting from existing functional electronic pacemaker as back-up in addition to benefiting from autonomic neural and hormonal input of the biological pacemaker and life-long battery. Because we are combining Phase I and II clinical studies we expect to enroll 10 patients with $220K cost per patient plus cost of production of the device. Based on existing reports of clinical trials with adenoviruses we do not expect immune response. If necessary defective biological pacemaker can be inactivated with currently approved orally bio-available medication.

Comparables – Device with no transvenous leads:
In June of 2012 Boston Scientific acquired Cameron Health who had been developing subcutaneous implantable cardioverter defibrillator. At time of acquisition the Cameron device was approved in Europe and was expected approval by the FDA during 2013. The agreement included an upfront payment of $150 million, payable upon transaction closing, an additional potential $150 million payment upon FDA approval plus up to an additional $1.050 billion of potential payments upon achievement of specified revenue-based milestones over a six-year period following FDA approval.

Comparables – Leadless pacemaker:
EBR Systems is developing a chronically implantable leadless cardiac pacing device for the treatment of heart failure. EBR benefited from four rounds of venture funding totaling $104 million. EBR Systems is performing feasibility studies with 35 patients in Europe.

Manufacturing: Transgene will produce the genetic construct for late pre-clinical and clinical development. The catheters for delivery of the genetic constructs will be provided by Celyad. We expect our product to be cost effective due to low production cost, endovascular delivery, speedier recovery post procedure and no need for future procedures focused on battery pack replacement.

Funding Strategy and Use of Proceeds:
Tranche I, months 1-18, $3M, optimization of genetic construct, selection of clinical candidate
Tranche 2, months 19-24, $800K, 6-month canine studies to generate PoP, preparation and prosecution of IND submission
Tranche 3, months 25-37, $1 Mproduction of GMP-grade material by Transgene for clinical development
Tranche 4, months 37 -50, $2.2 M for phase I/II studies with 10 patients