Chapter 1
Executive Summary

I. THE EXECUTIVE SUMMARY

I.A. Reasons For Conducting The Study

With well over $4 billion already invested, Angiogenesis Foundation, Inc[1] estimates Angiogenesis as one of the most heavily funded areas of medical research in human history. With the passage of Proposition 71 in 2004 committing $3 billion over 10 years,[2] State of California became the largest single source of funding for stem cell research in the world, followed by billions more committed by other governments. Tipped as the **Gold Rush of the 21st Century**, the biggest beneficiary of these initiatives that is closest to commercialization is by far "**Regenerative Cardiology"**.

Despite the magnitude of the investments, the initial euphoria of growing natural bypass to the blocked arteries was dampened by the statistically week or no efficacy reported in most of the FDA approved clinical trials. Major players in regenerative cardiology business who were bullish to begin with, transformed to bears. However, a second wave of clinical trials driven mostly by stem cell approaches to regenerate heart appears to be gathering the momentum. Surprisingly none of the countless published research reports so far investigates the reasons for the failed clinical trials that places at risk Billions invested in developing a viable heart repair therapeutic. This study fills that void.

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I.B. Study Goals & Objectives

The principal objective of the study was to provide comprehensive analysis of emerging approaches in regenerating / renewing dysfunctional portions of a diseased heart, identify problems that

[1] www.angio.org/patients/cancer/understanding_angiogenesis.html
[2] http://www.cirm.ca.gov/pdf/prop71.pdf

caused the disappointing clinical trial outcomes, and formulate answers to some of the difficult questions in the context of improving measurable efficacy in ongoing or future clinical trials. A point to be noted here is that there is another approach to growing coronary vessels in laboratory and then grafting them during a bypass surgery. Such ex-vivo approaches are in early pre-clinical stages, therefore not covered by this report.

In the changing paradigm adult heart is now largely seen as a Self-Renewing Organ. Such self-renewal broadly comprises of two anatomically distinguishable and physiologically integrated processes that build new blood channels to bypass the blocked arteries (**Angiogenesis**), and new myocardial tissue to compensate for the portions of dead myocardium (**Myogenesis**).

i. **The First Wave Lessons**
The first wave of clinical trials for growing coronary arteries began in mid nineties with much hype and expectations but ended in disappointment with the end of the millennium. It is the principle goal of the study to identify the problems and ascertain if they are insurmountable.

ii. **The Second Coming**
The second wave of clinical trials is now gaining momentum. It is an opportune time, and another goal of the study, to shortlist the issues based on the lessons learnt from the initial failures and address them.

iii. **Solution**
Finally, it is the goal of this study to formulate a strategy that maximizes the probability of achieving significant efficacy in the ongoing and future clinical trials.

Accordingly the report aims at forecasting near term measures based on an assessment of the merits and limitations of the various therapeutic approaches and their clinical development protocols. In essence the primary goal is to evolve a technologically sound strategy that will not only revitalize the currently active or on hold neocardiogenesis programs but also revive those terminated for reasons of insufficient or no efficacy.

I.C. Target Audience

This report explains the angiogenesis and myogenesis processes and the cellular mediators involved in their regulation in the context of designing therapeutic strategies to exploit human heart's newly discovered self-renewal qualities. It offers new insights needed to understand regulation of such self-renewal scenario, which we speculate is uniquely different than any of those encountered in any other drug discovery setting. The report articulates the impact of these novelties on treatment protocols, as well as their effects on the efficacy of the therapeutic agents in clinical development.

We hypothesize that just copying any conventional protocol ditto is not likely to produce the desired results. It is therefore an invaluable tool for business planners, investors and investor consultants, acquisitions specialists, licensing strategists, product managers, market research analysts, expert committees, regulatory approval committees, academicians and physician investigators involved and interested in regenerative cardiology.

I.D. Sponsorships

This research was neither sponsored by any of the known companies in therapeutic angiogenesis / regenerative medicine business, nor was any part of it funded by any party actively engaged in ongoing regenerative cardiology research. All the resources used for this research were raised and contributed in-house by MetaReports.net.

I.E. Scope & Format

The scope of this study is limited to application of principles of regenerative medicine to therapeutic angiogenesis and myogenesis in treating patients of coronary artery disease. More particularly the research delves into ways of resolving the less than desirable outcomes of the clinical trials with several therapeutic agents conducted in the recent past. The format is therefore more akin to scientific exposition rather than to equity research. Any equity valuation is meaningless if the technical foundations on which products are built aren't robust. The happenings of the recent years in this field have indeed put that robustness into question. Since most forecasts published so far on regenerative cardiology companies have been so much off from reality, we rather refrain from projecting any hypothetical equity valuations at this time. This report is therefore technology focused rather than equity focused. Nevertheless, a fairly comprehensive coverage of the Neocardiogenesis Landscape is provided. Brief profiles of companies associated with products that grow new heart tissue (both in-vivo and ex-vivo) are sufficiently illustrative of their place in the regenerative cardiology marketplace.

I.F. Methodology

We deploy a unique proprietary methodology to eliminate all possible sources of biases and prejudices that are inherent with any sponsored or paid research. Pursuant to our proprietary MetaReports technology the research is conducted at our own behest based on popularity, recommendations, unmet need, urgency of the subject matter, and our own in-house expertise. The completed Research Report is presented to the audience in two phases:

a) Dynamic Phase

During the dynamic phase the report is initially released as a dynamic living document for 90 days. During this phase all the subscribing parties who are mentioned in the report are entitled to an opportunity to edit the contents relevant to them by commenting, updating, modifying, correcting any text they find erroneous or inadequate or incomplete. Such edits are however moderated by the author or the chief editor of the report.

b) Final Release

The final release of the report includes all the edits received from the initial subscribing audience and moderated by the moderator of the report. The final release is provided at no extra cost to the original subscribers. For further details on MetaReports methodology please feel free to contact us at info@MetaReports.net .

I.G. Information Sources

Peer reviewed journals are the major source for the scientific expositions

deployed in this research. The sources for corporate, statistical, administrative and regulatory information on companies, academic institutions, governmental or non-governmental outfits include Internet, press releases, media articles, analyst reports, regulatory filings and disclosures, and other sources in public domain, such as company annual reports and 10-Ks, minutes of meetings, prospectus etc.

I.H. Related Projects by this Publisher

Several related research projects in Cardio Series are currently underway at MetaReports.net. Following MetaReports are in pipeline in the next several months.

1. Cardiac Monitoring - The Changing Landscape Of Cardiac Care
2. Endothelial Dysfunction – Mother Of All Cardiovascular Maladies
3. Plaque Regression and Stabilization – The Next Frontier In Coronary Artery Disease
4. Stents – The Odyssey Continues

An updated list is also available at www.metareports.net

I.I. Conclusion

The study not only achieved all of its goals, but discovered in serendipity the novelty of the neocardiogenesis phenomenon that sets it apart from any of our drug development experiences of past or present. This is the first ever research report that identifies the specific problems that failed the clinical trials of regenerative cardiology products, determines that those problems are not insurmountable, and formulates elaborate solutions to solve them. It is also first ever in that serendipity found a new abode - Market Research. This project culminated in at least three patents either filed or under preparation.

With an unprecedented 80 plus companies involved in regenerative cardiology's Second Coming, and the success still eluding, the timing of this research report is opportune.