

# Metavo L.L.C.

## Executive Summary



Metavo Life Sciences Inc. and Metavo LLC, a Texas Limited Liability Company (“Metavo”) is a new venture based on science to delay the physiological changes associated with aging. Metavo was formed to develop and market products to maintain health, body functionality and well-being by aiming at the root molecular causes of the aging process. Many natural products exist that improve health and extend lifespan. <http://www.uttx.com/metavo.html>. These natural molecules modulate cells and tissues to extend the period of healthy, functional, independent existence. Metavo is utilizing technologies that improve and extend healthy existence and expects to translate these technologies into marketable products to delay, with the hope of avoiding, the debilitating conditions that are considered ‘normal’ in old age. Metavo has a provisional funding commitment of matching investment money from CentreStone Ventures LP, a Canadian Life Sciences focused venture capital fund, up to US\$ 1.0 million.

Metavo was formed under the guidance of Genesys Venture Inc.. [GVI] is a company dedicated to the development of biotechnology ventures. <http://www.genesysventure.com> Genesys Venture Inc. (“GVI”), Winnipeg, Canada, provides the expertise, experience and energy required to manage emerging health and biotechnology ventures. Led by bio-entrepreneur Dr. Albert Friesen, the GVI team has extensive experience in helping to develop innovative life-sciences companies and presently has mentored a stable of several public companies. The most notable companies being Mantex, Inc. now part of Gilead Sciences Inc. and Medicure, Inc., a public cardiovascular pharmaceutical venture having a market capitalization of over \$145 million. The latest GVI company, Diamedica, Inc. is [Jan-Feb 2007] pursuing an initial stock offering [IPO] on the Toronto Stock Exchange.

The driving force behind Metavo is Geoffrey Grant, Ph.D. <http://www.uttx.com/Grant.html> an emeritus professor, biochemist and expert on aging who has extensive experience commercializing university based technologies. Dr. Grant has been a scientist at the Salk Institute, a successful entrepreneur and most recently a technology development business manager at the University of Texas.

Metavo technologies are being licensed from several renown research institutes, the most notable being the Salk Institute in San Diego, CA. In his laboratory at Salk, [Dr. David Schubert](#) has spent a lifetime working on the preservation of the brain and nerve cells, and, in particular, have focused upon solutions to the neural and cognitive decline in Alzheimer’s disease. The laboratory has developed pharmaceutical molecules that are related to, but 100-1000 times more active than, the bioflavonoids [such as fisetin and biacalein], the polyphenol, resveratrol, and the Indian spice, curcumin. These molecules are natural ingredients found in a wide variety of fruits, vegetables as well as exotic plants. They have been shown over the past decade to have a wide range of medicinal properties that include the ability to inhibit cancer cell growth, block inflammation, reverse plaque formation in Alzheimer’s models [[Scientific American, Feb 2007](#)], protect nerves cells from toxins, enhance memory and cognitive abilities and most recently [[Nature, Nov 2006](#)] resveratrol significantly extends the lifespan of rodents. These natural compounds, to be clinically active, require dose levels much higher than the levels found naturally in plants. Their medicinal use, therefore, requires either chronic consumption of plant

**“It’s Never Too Late To Rejuvenate”**

# Metavo L.L.C.

## Executive Summary

extracts over long periods and/or isolation and purification of the active ingredients so that higher doses can be administered. A clinical trial with curcumin on Alzheimer's disease is presently being conducted at UCLA [ClinicalTrials.gov identifier NCT00099710].

The Schubert laboratory at the Salk Institute has had synthesized curcumin derivatives of the natural molecules that are 100 to one thousand times more active than the natural curcumin plant compounds, depending upon the assay method, functioning as neuro-protective agents in culture. These molecules are being patented as pharmaceuticals and being tested for both possible toxicity [none shown in culture] and for their efficacy in animal clinical models, such as Alzheimer's disease, by the Cole laboratory at UCLA [referenced in the Scientific American article [attached]; and the clinical trial; see above] and in cognition and memory tests by independent laboratories. These synthetic [modified natural compounds] appear to have the potential of high potency cutting edge pharmaceuticals, the next generation prevention and treatment for the diseases of aging. The pharmaceutical giant, Novartis, has already expressed interest in these molecules.

Funding of the Metavo venture has been arranged with Centrestone VC group, a Canadian government-backed venture capital fund who have agreed to provide matching monies up to US \$1.0 million. The alternate matching \$1.0 million will be raised by Metavo LLC., in which member/partner interest increments are restricted to \$25,000 minimum each-to be escrowed until \$500,000 is available. The principal initial use of funds is to further the research of the molecules in animals and establish their potency and efficacy as therapeutics. The long term goal, exit strategy, is to attract the attention of 'Big' Pharma and either joint venture or sell the pharmaceutical licensing rights.

Presently, NO drug is prescribed to prevent or cure Alzheimer's. The compounds that are FDA approved and medically prescribed to treat Alzheimer's are all directed at symptomatic relief not at solutions to the condition. There are only four drugs that the FDA has approved and that are currently available for relief, but not to cure patients with Alzheimer's in the United States; Tacrine (CognexR), Donepezil (AriceptR), and Rivastigmine (ReminylR) that inhibit acetylcholinesterase. and the fourth, Memantine (NamendaR) that prevents glutamate excitotoxicity.

The molecules from the Salk Laboratory are potent and unique. The Salk patented molecules show an ability to promote the destruction of the Alzheimer's plaque  $\beta$ -amyloid protein in cell cultures and therefore we consider the molecules to have the potential to prevent and reverse the neuro-degeneration that are prevalent in Alzheimer's disease.

**“It's Never Too Late To Rejuvenate”**

# Metavo L.L.C.

## Executive Summary

### Biotechnology Investment Risk & Reward Factors

Alzheimer's disease progressively destroys a person's memory and ability to learn, reason, make judgments, communicate and carry out daily activities. It affects more than 4 million Americans and as the population ages Alzheimer's disease will double in next 20 years. FDA approved Alzheimer's pharmaceuticals do not reverse or slow down disease progression but have worldwide annual sales of US\$3.1 billion. The Alzheimer's pharmaceutical market is expected to grow significantly with the arrival of products that have the potential to alter disease progression.

The development of a pharmaceutical drug involves substantial risk and the process ultimately requires many years of extensive research and clinical trials (Figure 1). However, if drugs are developed that show potential, the pharmaceutical industry has a solid track record of investment (Figure 2). The present level of R&D investment in drug development by the pharmaceutical industry totals over \$30 billion dollars per year.

Figure 1:

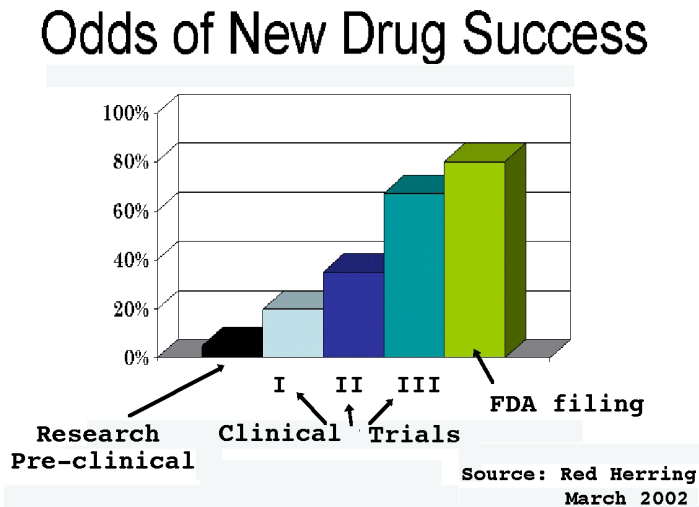
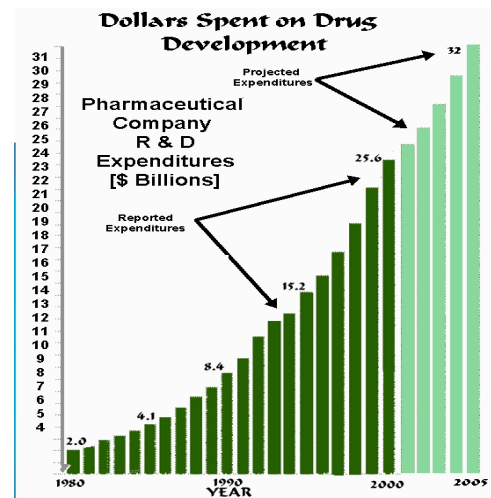


Figure 2:



Drug development is a long, involved and expensive process (Figure 3). The research must discover a substantial breakthrough in the activity of new compounds and be able to demonstrate reproducible results at all levels of testing. In general, this involves extensive screening of molecules that have potential and then customizing the most active candidates by specialized chemistry to perfect the activity desired.

Figure 3: Drug Development Process

- **Drug Discovery** ~3 Years
  - Identify or validate genes, Identify or validate drug targets, Develop cell assays, Discover/develop small molecules, Show efficacy
- **Pre-Clinical** ~ 2.5 Years
  - Pharmacology, Toxicology, Formulation of drug form, Pharmacokinetics
- **Clinical** ~5.5 Years
  - Phase I – Safety & Dose
  - Phase II – Efficacy & Side Effects, Multiple Dosages, Prove Concept
  - Phase III – Reactions & Long-term effects
- **Submission to FDA for approval** ~ 1.5 Years
- **FDA Approval**

**“It’s Never Too Late To Rejuvenate”**

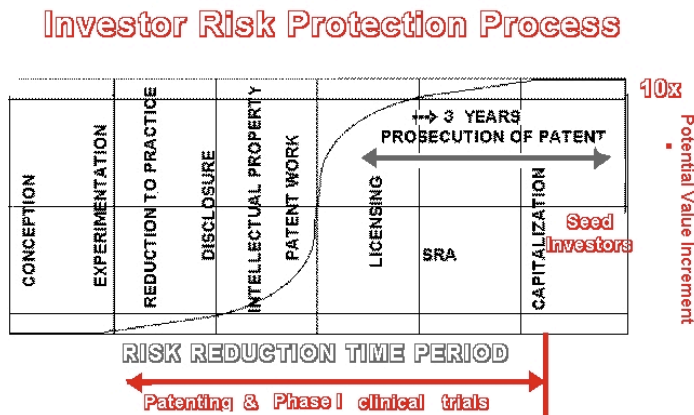
# Metavo L.L.C.

## Executive Summary

Once a molecule of interest has been identified it must be protected through the patenting process. This means the molecule must be unique, have specific utility as a therapeutic agent and not be obvious in its design to experts in the field. It generally takes several years until a patent is issued during which time the first stages of animal testing usually take place. Efficacy in animals is essential together with studies to show the molecule is non-toxic when administered at levels expected to provide therapeutic results.

The patenting and animal testing stages of drug development are designed to reduce the risk to the investors and to attract the interest of the big pharmaceutical companies to the potential of the discovery. This is a critical stage, representing a significant potential value increase to early stage investors (see Figure 4). When a compound has shown efficacy in cell culture and animal experiments it proceeds to human clinical trials.

Figure 4:



It is critical that testing must be done to show that the therapeutic value is functional on animals then upon small groups of humans. The testing must show that the drug is both effective as treatment and has no adverse effects or toxicity when administered to patients. As the testing continues through the clinical trial process, the potential value of the drug increases proportionately. It is a common strategy for companies to seek licensing partners, joint cooperative

ventures or outright sale of the discovery as the value and potential return to investors increase (Figures 5&6) and the costs continue to rise. Often times, a deal must be arranged to facilitate the final stages of drug development. As a benchmark, a phase III clinical trial can require in the range of \$50-\$100 (or more) million to conduct and demands thorough conclusive evidence of potential success as a therapeutic drug.

Figure 5:

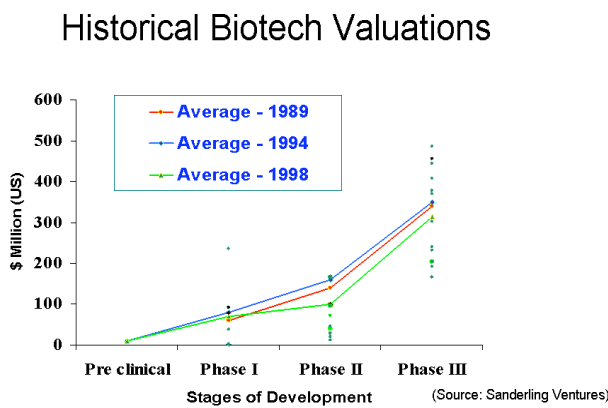
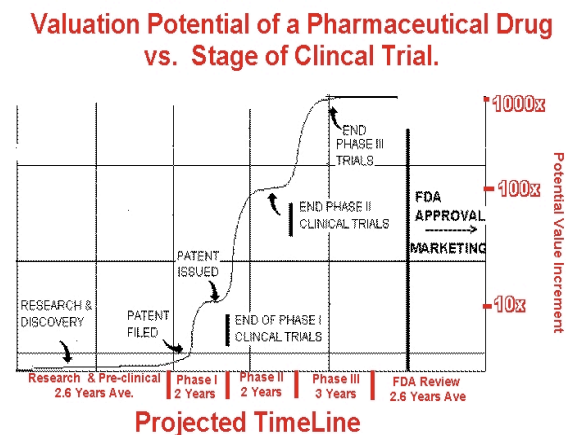


Figure 6: Source PhRMA (2001)  
Tufts CSDD Approved NCE Database.  
DiMasi et al. J. Health Economics 22 (2003) 151-185



“It’s Never Too Late To Rejuvenate”