



**Cycle Dose Modifier<sup>™</sup>  
for Advanced Pharmacotherapeutics<sup>™</sup>**

**CURRENT MEDICAL CHALLENGES**

Recent reports from the Institute of Medicine have found that drug dose irregularities have resulted in thousands of deaths, innumerable and extended hospitalizations and Billions of dollars of costs each year.

Drug doses are based upon a 'One-size-fits-all' model which results in various degrees of effectiveness, wasted spending on medicines that don't work and potentially dangerous adverse effects in many medications such as anticoagulants (blood thinners), antidepressants and other complex therapies. Our solution can be used for any drug, any disease and any patient; we will first focus on oral anticoagulants; Coumadin (brand name) and Warfarin (generic version).

Blood thinning drugs are widely prescribed for many different conditions and may be taken for life in heart disease and stroke or for extended periods during joint surgery. Oral drugs for thinning the blood have no clear relationship between the dose and the drug's effect and are considered 'Non-linear'. If the patient receives too little drug it may result in blood clot formation and too much drug results in bleeding; both untoward and potentially deadly effects. Many drugs and conditions result in changes of the effect of the drug on the thinning of the blood and the basic process of how the drug works, by irritating the liver changes dynamically in each patient as well.

These dosing irregularities and misadventures during blood thinning therapies result in:

- Significant patient discomfort
- Repeated patient doctor visits
- Numerous lab tests
- Prescription changes
- Serious adverse events and complications (bleeding and/or clotting)
- Annual increased costs that exceed \$9 Billion

New dosing strategies based upon the patient's genetic information provide some improvement but only during the initiation phase of treatment, not during maintenance and only by about 40%.

Physicians and specialized prescribers, focused algorithms and newly devised genetic based dosing strategies have accuracies less than 50%, to give the patient the correct dose to result in the laboratory defined level of blood thinning needed.

An improved system to accurately dose blood thinning therapies would benefit patients, prescribers, healthcare facilities, payers and drug manufacturers. The system would have to include better dosing, the new genetic findings, control lab studies and be applicable in all phases of care by the patient, prescriber and facility.

#### OUR OPPORTUNITY

A comprehensive multi-phasic drug dose modification system that can individualize drug doses to achieve specific targeted lab values, include genetic data for initiation of therapy, control the timing and validity of lab studies to base dose changes on and resulting in a dose to marker value accuracy greater than 90%

- **Cycle Dose Modifier is a proprietary multi-part computer based system that;**
  - **Directly relates the drug dose to the lab marker value**
  - **Allows concurrent adjustment for all unique individual patient characteristics (Inter-Individual Variability)**
  - **Accommodates genomic lab values upon initiation of therapy if available**
  - **Controls lab value sampling times for validity of dose changes**
  - **Can be utilized in any healthcare setting by the prescriber or the competent patient**
  - **Is able to manage multiple agents and markers of efficacy and toxicity and to support the transition between agents such as acute blood thinning with injectable drugs, heparins and the oral anticoagulants**
  
- **Results in;**
  - **Improved safety and effectiveness**
  - **Faster time to therapeutic range and levels**
  - **Fewer adverse events**
  - **Longer time in the therapeutic range and level**
  - **Lowered treatment costs**
  - **Reduced lab studies**
  - **Reduced number of care visits**

We have devised a proprietary (US, PCT and EUR patents pending) drug dose modification method that relates a drugs dose to achieve any specific level of a lab test result (biomarker value), control for Inter-Individual Variability, identify each drugs effect on the marker and manage the sampling of the biomarker used. The method, Cycle Dose Modifier™ has an accuracy greater than 90% and can be used in any drug, any patient, with any disease and with any marker.

This method allows us to extend proprietary patent protection to a drug in several ways by adding it to the drug(s) as part of the label.

## MARKET POTENTIAL: ORAL ANTICOAGULANTS – COUMADIN (WARFARIN)

- About 20 Million patients take the drug each year in the U.S.
  - More than 500,000 new patients are added each year
- Dosing irregularities during the initiation and maintenance of Coumadin therapy result in adverse events (bleeding and/or clotting) and costs that exceed \$9 Billion
- The accuracy of current Coumadin dosing methods is less than 50% the accuracy of Cycle Dose Modifier™ is greater than 90%
- Dose modification of oral anticoagulants has been one of the most challenging and daunting aspects of medicine for prescribers and patients
- Current methods assist during the initiation phase of treatment but not after the first month of therapy

### PRODUCT

Cycle Dose Modifier™ is a multi-phasic software system that is custom built for the dosing of Coumadin (Warfarin) and its primary lab marker the INR and is integrated into any computerized platform; PDA, portable, network or desktop. Any drug or combination of drugs is an individual product opportunity.

The prescriber enters the previous cycle drug dose and lab value, the current cycle drug dose and marker and the desired marker value, then the system calculates the dose to achieve the desired marker.

### STRATEGY

Through initial outside funding of \$200K, (the principles have invested in excess of \$500K to date) we will submit the new system for FDA review and approval under 510(k) and develop the business units.

We have already had an earlier version of our technology approved by the FDA as a Class II medical device, 510(k) for drug dose modification and will submit the current version for approval, (a ninety to one-hundred and twenty day process); there are no other FDA 'approved' devices and or methods.

We have already begun to work with multi-national pharmaceutical manufacturers in the drug development process by demonstrating efficacy in a blinded dataset (see attached data). We envision individual business units based upon specifically targeted market areas of drug use based upon specialty and site of use to include;

- Hospital
- Physician offices
- Out-patient clinics
- Patient self-care
- Long-term care

Based upon market research into each of these targeted phases of care and specialty application areas; (cardiac: heart attack and atrial fibrillation, stroke, thrombosis, cardiac surgery, joint surgery) we will identify the variations of presentation, features and benefits to support integration and commercialization.

During this research phase we will develop the subject matter, marketing and sales expertise to design, develop and head each of the five proposed business units.

COMPETITION

While there are various other approaches to this problem none have been successful or commercially offered. Traditional pharmacokinetics and pharmacodynamics have not been effective in blood thinning agents. Innumerable dosing systems have been developed but not submitted or approved by the FDA and only result in accuracies less than 30%.

Recent advances in genetic based dosing have demonstrated some improvement during the initiation phase, about 40% accuracy of dose to marker.

BARRIERS TO ENTRY

Our primary protection comes from a series of US, PCT and EUR patents currently pending. Our US Patent counsel is; Bracewell – Giuliani, European Patent counsel is; Marks & Clerk.

Secondary barrier to entry is our FDA strategy and success.

MANAGEMENT TEAM

There are two primary team members, the technology inventors, with extensive and successful pharmacologic, clinical and business experience who have worked together in previous ventures. Both have heavily invested in the project.

Additionally we have recruited experienced sales, marketing and geneticists to the team.

USE OF PROCEEDS

We are seeking \$200K in equity funding to build upon the existing IP, file the FDA 510(k) registration, to develop the business units and to establish refine the marketing and sales strategy (see attached schedule). We anticipate five to six months time to complete this phase of operations then to move on to full commercialization through additional funding of ~\$3M.

ROI/EXIT STRATEGY/VALUATION

We anticipate \$3 to \$5 Million annual returns from each business unit. Exit strategies include various liquidity events such as licensing and acquisition. Valuation is based on a fraction of the independent appraisal of the IP at \$25M.

CONTACT INFORMATION

For more information contact; Michael G. Singer (989-724-6645) and John D. Kutzko, (941-485-8882)

CDM	
Mean	109
Standard Deviation	29
Correlation	0.92
Median	104
N	64

**Figure 1: Accuracy of Cycle Dose Modifier**

These data reflect the use of the Cycle Dose Modifier™ to dose coumadin in sixty-four patients participating in a retrospective study using only the first part of the system. Additional studies utilizing the complete system demonstrate an accuracy of 94% with a Standard Deviation of 8%

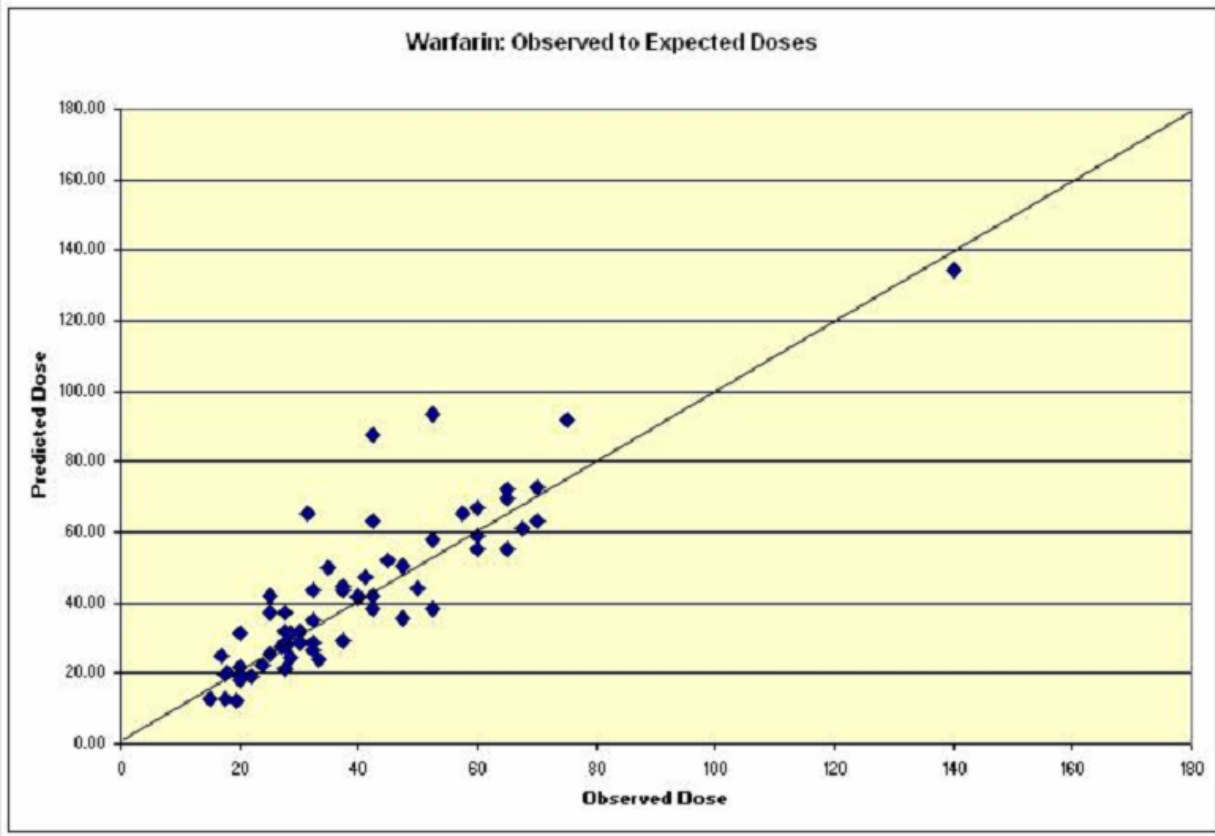


Figure 2: Chart of Above Data

INITIAL PROJECTED BUDGET AND 150 DAY TIMELINE

*Advanced Pharmacotherapeutics: Warfarin*

Parties	Company	Status	Number	Total Cost
Michael G. Singer	Petra Biotek	Principal	1	\$25,000.00
John D. Kutzko	Petra Biotek	Principal	1	25,000.00
Skip Kaplan	Kaplan Medical Associates	Principal	Company	25,000.00
Annette Taylor	Kimball Genetics	Partner	Company	0.00
FDA Consultant	Smith and Asoc	Contractor	Company	8,000.00
Programming	VJC Communications	Contractor	Company	10,000.00
Legal	To Be Determined	Prof Serv Prov	Practice	11,000.00
INR Device Manufact	TBD	Vendor	Check two or three	6,000.00
Marketing	TBD	Contractor	Company	12,000.00
Technical Research	TBD	Contractor	Specialty Focus (multiple)	11,000.00
Travel	As needed			12,000.00
Presentations	TBD	Contractor	3 X-Plane	25,000.00
Demo Equipment	TBD	Manufacturer	PDA's	5,000.00
FDA Filing Fees	FDA CDRH	Regulatory	Division/none recurring	4,500.00
Miscellaneous	As needed			7,500.00
<b>TOTAL</b>				<b>\$187,000.00</b>

Figure 3: Proposed Use of Proceeds Initial Outside