About Metabolon

Advancing the field of metabolomics by pioneering and patenting the industry’s leading biochemical biomarker discovery and profiling platform

- **Initial funding in 2003, raised $45 million to date**
  - Sevin Rosen, Harris & Harris, Syngenta Ventures, Aurora Funds, Fletcher Spaght, Fulcrum Financial, Keating Capital Inc.
- +60 million in bookings to date
- +100 staff (40 PhDs) in Research Triangle Park, NC
- Transformational technology marries software, know-how and biochemical biomarker discovery
Company Key Points

- Validated, pioneering technology poised to transform disease treatment and diagnosis
  - Strong IP protection with more than 100 patents filed, 17 issued

- Profitable Metabalytics™ division growing rapidly with high repeat business from a Who’s Who of pharma and biotech
  - Ex-U.S. expansion provides further growth opportunity

- Technology and know-how also being applied to rapidly develop a robust diagnostics pipeline
  - Products help prevent disease with significant long-term costs, or affect patient management
  - Targeting 2 largest markets: type 2 diabetes and oncology

- +50 peer-reviewed scientific papers published in the last 3 years.
Two Commercialization Paths

Metabolytics

Biomarker Discovery
• mVision
• mView
• mSelect

Biomarker Monitoring
• mFocus
• Quantose IR

BioProcessMonitoring
• COP

Diagnostics

Pipeline
• Quantose
• Prostarix DRE
• Prostarix
• Bladder cancer aggression
• RCC aggression

Patient Monitoring
• Cisplatin

Pharma, Biotech,
Nutrition, Agri,
University, Org

2010 $14 Million
2011 $20 Million

Physicians and Patients

Long-Term Value Creation

ATP

NAD+

NADH

Bladder cancer aggression

RCC aggression

Cisplatin

Prostarix DRE

Prostarix

Pipeline

Pharma, Biotech,
Nutrition, Agri,
University, Org

2010 $14 Million
2011 $20 Million

Physicians and Patients

Long-Term Value Creation
Focus on Metabolism

Biochemistry Advantages
- Any sample type
- Many applications
- Fewer total biochemicals

Solutions through Understanding Metabolism

DNA
RNA
Proteins
Metabolism
Disease Mechanism

Metabolites:
- glucose
- cholesterol
- L-threonine
**Global Effects on Metabolism**

**Disease Biomarkers**

**Mechanistic Toxicology**

**Drug MOA**

**Cellular Characteristics**

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**Data Interpretation**
- 100’s of Studies
- Institutional Knowledge
- Expert Biochemists

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**Metabolon Platform Technology**

**Metabolon Platform Technology**

**Biochemical Extraction**

**UHPLC-MS/MS (+ESI)**

**UHPLC-MS/MS (-ESI)**

**GC-MS (+EI)**

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**Metabolyzer™**

**Peak Detection**
- 15,000 ion features

**Peak Integration**
- 15,000 ion features

**Library Search**
- 15,000 ion features

**QA/QC**

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**Statistical Analysis**

**Heat Maps by Pathway**

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**UHPLC-MS/MS (+ESI)**

**UHPLC-MS/MS (-ESI)**

**GC-MS (+EI)**
- Methods - Fundamental IP provided by pioneering patents, first filed in 2000
- ‘Stepping Stone’ Patents - Data analysis and analytical platform inventions
- Growing Biomarker Patent Portfolio:
  Issued and Pending patents for biomarkers of toxicity and diseases including:
  - Cancer, Insulin Resistance, Liver disease and Liver toxicity
Metabolytics Business
Significant Customer Growth

$60MM Cumulative Bookings
Metabolytics Business
Financial Growth

45% CAGR

Revenue
EBIT
GM%
Who’s Who Customer Base

Biomarker Discovery
• mVision
• mView
• mSelect

Biomarker Monitoring
• mFocus
• Quantose IR

BioProcess
• COP

Pharma, Biotech, Nutrition, Agri University, Org
Diagnostics Business Strategy

• Quantose™ insulin resistance test developed through commercial partnering and targeted business segments

• Develop a fully integrated diagnostics business utilizing our understanding of cancer metabolism
Current Glycemic Diagnostics Do Not Measure IR

Current glycemic diagnostics do not measure insulin resistance (IR). Normal fasting plasma glucose (NGT) does not diagnose early IR, and early IR is not reversed. Pre-diabetic stages are critical for early intervention, and middle stage IR is potentially reversible with lifestyle changes. Late stage IR progresses to type 2 diabetes (T2D) with vascular damage increasing and β-cell function diminishing. Pre-diabetic stage with cardiovascular disease (CVD) complications is also a critical stage. Diagnostic tests for insulin resistance include FPG, OGTT, and A1C.

- NGT-IS: Normal Glucose Tolerance Test
- NGT-IR: Insulin Resistance Glucose Tolerance Test
- IGT: Impaired Glucose Tolerance
- T2D: Type 2 Diabetes
- Pre-Diabetic
- Normal
- 100 mg/dl: Pre-Diabetic Fasting Plasma Glucose
- 125 mg/dl: Diabetic Fasting Plasma Glucose

T2D patient with disease 5-7 yrs on average when first diagnosed.
33% of the population in the developed world considered "at risk"

Quantose peak royalty revenue potential ~$300M if one third of at risk patients get tested annually in the US alone
Fasting plasma test to determine the risk of diabetes in 5 years

Monitors biomarkers for insulin resistance discovered and validated in collaboration with top internationally recognized KOL’s

Earliest indication of Type 2 diabetes

Measures the current status of IR and how that affects diabetes risk.

Monitors health improvements from life style and drug interventions.

Targets “at risk” patients with BMI of 26 to 32

5% of patients monitoring their risk with Quantose improve their condition through more aggressive intervention

More effective than any other measure in changing patient outcome
Cancer Diagnostics Business Strategy

• Develop a fully integrated diagnostics business utilizing our understanding of cancer metabolism

• Tests focus on treatment management of cancer patients
• Target significant underserved medical needs
• Reduce healthcare costs while improving patient care
• Build internal salesforce to call on urologists/oncologists
• Run tests through CLIA laboratory to ensure quality, capture economics, build customer relationships
Warburg made a striking discovery in the 1920s that, even in the presence of ample oxygen, cancer cells prefer to metabolize glucose through non-oxidative pathways (aerobic glycolysis) – Warburg effect.

This insight has yielded seminal practical applications such as FDG PET for tumor imaging.

However, for many years, Warburg effect largely viewed as a reflection of a function of the hypoxic tumor environment.

Research continued but was eventually eclipsed by a captivating finding from a parallel track of cancer investigation .........
Upon the discovery of oncogenes, the molecular biology explosion surpassed Warburg’s line of inquiry for all but a small group of investigators. Eventually, a realization that Warburg’s findings and cancer activating mutations were intimately connected.
Warburg Effect

fructose 6-P → glucose 6-P
fructose 1,6-bisP → 1,3-bisphosphoglycerate
glyceraldehyde 3-P → 3-phosphoglycerate
2-phosphoglycerate → phosphoenolpyruvate → pyruvate → lactate

TCA cycle

12 metabolites

~100 metabolites
**Diagnostics Product Pipeline**

<table>
<thead>
<tr>
<th>Diagnostic Product</th>
<th>Indication / Estimated Annual Market Size</th>
<th>Business Case</th>
<th>Feasibility</th>
<th>Validation</th>
<th>CLIA Ready</th>
<th>Market Ready*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prostarix™DRE</td>
<td>Guide prostate biopsy decision / $600 mil.</td>
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<td>Prostarix</td>
<td>Prostate cancer aggression / $619 mil.</td>
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<td>Vasicar™</td>
<td>Bladder cancer aggression / $168 mil.</td>
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<td>2013</td>
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<tr>
<td>Cisplatin toxicity</td>
<td>Cisplatin treatment tolerance / $200 mil.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2013</td>
</tr>
<tr>
<td>Renal Cell Carcinoma</td>
<td>Kidney cancer aggression/ $70 mil.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2013</td>
</tr>
</tbody>
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* Commercial launch is pending financing
Company Summary

- Validated, pioneering, patented technology poised to transform disease treatment and diagnosis

- Over the past 5 years, rapidly growing metabolytics business. 320 studies completed in 2010 processing over 33,000 samples. +60m in bookings since inception.

- Technology and know-how applied to develop a robust diagnostics pipeline targeting the largest healthcare disease categories.

- Large scale biology studies (clinical, GWAS) started in 2009.
**Study Rationale:**

Using Metabolon’s Global Metabolomics to Phenotype Two Large Genomic Studies

- **KORA Genomic Study**
  - 1,768 individuals
  - 655,658 autosomal SNPs
- **TwinsUK: (Merlin) Genomic Study**
  - 1056 individuals
  - 534,665 autosomal SNPs

28 genomewide significant associations to biochemicals \( (p<2\times10^{-12}) \) in the discovery study

\[ \rightarrow \text{27 fully replicated in second study} \quad (p<2\times10^{-5}) \]