Business Model

- GenoMed is now effectively private
  - Drug Discovery needs $7.5 M
  - DNA Diagnostics needs $2.5 M
  - Disease Management needs $0
- Exit strategy: IPO (or sale of a drug)
- Expected ROI: >200% over next 3 years
Unique Advantages

- **SNPnet™**
  - versions 1.0 (13,000 SNPs) and 2.0 (80,000 variants, covering the entire genome)

- Access to patients’ labs and charts for disease-gene discovery

- Drug design, synthesis, & testing partners: least expensive in the world
I. Drug Discovery

- We’re unique in having found **germline** SNPs for cancer
  - 5,000 SNPs per cancer
  - Roughly 2 SNPs/gene, i.e. 2,500 genes
  - Breast, colon, lung, ovary, pancreas, prostate, i.e. 2/3 of cancer in Caucasians excluding skin cancers
  - Our SNPs can predict who’ll get which cancer (predictive diagnostics)
I. Drug Discovery

- Our germline genes make the best drug targets
  - They operate earliest in the disease pathway
  - Unlike tissue-expressed genes, which operate years after the disease began
  - But which everybody else is using as drug targets
Why are germline genes better?

- Variation in germline DNA is where all disease starts
  - Cancer patients overexpress oncogenes and underexpress tumor suppressors beginning in their germline DNA
  - Mutations in tumor DNA are “private”
  - Each tumor is a “snowflake”

- Tumor-expressed genes can be compensatory, not causative
  - “Passengers, not drivers”
  - We have the drivers
Why are germline genes better?

- A disease pathway is like a river with ever larger waterfalls
- Amplification at each biological step may be 1,000 X
- It’s easiest to stop a river at its source
Biological Pathways: a series of cascades with huge amplification at each step
Disease Pathway: best hope lies in blocking earliest step
Tumorigenesis SNPs

- Using a SNPnet™ covering only 1/3 of the genome, we found about 2,500 genes associated with each of 6 different cancers in whites
  - Nobody else has found any yet
  - This will change in 2-3 years
- We estimate 10,000 genes per cancer
- What cellular program takes up 1/3-1/2 of the genome?
Tumorigenesis SNPs

What program takes up >1/3 of the genome?

• Differentiation...

Does sporadic cancer arise when a tissue stem cell fails to differentiate?

• In the embryo, the surrounding tissue expresses “fields” of powerful transcription factors.

• Not so in adult life: a proliferating tissue stem cell is literally on its own.

• Like driving without street signs (Boston...)
Tumorigenesis SNPs

We have the key to effective “differentiation therapy”

- Ideal for patients with stage 3-4 cancer
- Examples of differentiation therapy: 1,25-vitamin D and retinoic acid

Repurpose already existing, commercially available drugs into non-toxic, patentable cocktails based on the tumorigenesis genes we’ve found.

- New drugs will take longer and more $$
GenoMed’s Goal: “Kind” Chemotherapy

- Non-toxic but more effective treatment for late stage disease, a totally untapped market
- GenoMed’s 2,500 cancer-causing genes: ½ are oncogenes, ½ are tumor suppressors
- Design inhibitors to oncogenes
- Screen 1st for toxicity; genomic epidemiology guarantees clinical efficacy
- Many targets, so we can afford to throw most away, unlike other biotech or pharma companies
  - NB. 99.9% of drugs fail because of toxicity...
  - With 1,000 targets, at least 1 is guaranteed to survive toxicity screen
Cutting costs:

The “peer-reviewed virtual pharmaceutical company™”
GenoMed’s Virtual Pharmaceutical Company

GenoMed + academic labs + struggling biotech cos.

- Premise: cutting-edge science is hard to evaluate
- So let other scientists do the vetting
- Scientists don’t waste their time on bad science
- A credible team of scientists is the best validation for GenoMed’s scientific approach
- Academic labs, unlike Research Pharma labs, are inexpensive
I. Drug Discovery: 1st Project

- PTK6 (BTK) assoc’d w/ 4 cancers
- Chemmodeling, LLC designed 4 inhibitor structures
- Academic colleague at Natl Univ of Singapore (NUS) synthesized them
  - Including 15 analogues of cpd #2
- Next: in vitro testing
- NUS will submit the patent (normally $100K)
I. Drug Discovery: 1st Project

- BTK inhibitors are doing very well in the clinic.

- 1/4 share of IP for each partner:
  - NUS, Colleague at NUS, Chemmodeling, GenoMed

- More cash for GenoMed will allow us to keep a bigger share of the IP

- Value of a drug: $25-50M after Phase I, $500M after Phase III
I. Drug Discovery: Funds Requested

- **$7.5 million**
- Focus on targets involved in multiple cancers
- We have two sets of targets that are 1\(^{st}\) in class: nobody else has published them
New Drug Discovery

- Cheapest method is smart molecule design, as we’re already doing for BTK inhibitors.

- A business strategy for when we have more money:
  - Pick unknown targets—smart molecule design won’t work.
1st in Class Drug Discovery

- Overexpress gene product
- Look for binding, e.g. by surface plasmon resonance (SPR)
  - Use fragment-based libraries, or large libraries and high-throughput screening
- Expensive but w/ the biggest pay-off
- Will have to wait until we have sufficient capital
  - Or SPR, screening cos. are willing to share risk with us
Business Plan for New Drugs

- File patent on each drug structure
- Spin off separate LLC for each drug structure
  - Take in additional investment for each drug so as to limit dilution into GenoMed as a whole
  - Use cash for synthesis, toxicity testing, in vitro efficacy testing, etc.
  - As data mounts, risk decreases, and investment buys less
II. Disease Management

- Has been producing revenues since Dec, 2002 ($100 per patient)
- Now generating on-line revenues via PayPal
- 1 billion potential patients w/ HTN, diabetes (preventing dialysis)
- Repurposing drugs for cancer would mean additional patients ☟
II. Disease Management (cont.)

- Only marketing (publicity) is required
- Market size: 95 million Americans
  - High blood pressure, diabetes, emphysema
- Potential US revenues: $100/patient
  x 95 million patients = $9.5 billion
II. Disease Management (cont.)

- Making the world dialysis-free by 2020

- Market size: 1 billion adults
  - High blood pressure (Africa), diabetes (300M in India, 300M in China)

- Potential revenues: $10/patient, or $10 billion

- Could be delivered cheaply to Third World via cell phone & computer
Diseases with Published Superior Outcomes

- Early on, chronic renal failure can be reversed, i.e. 90% of ESRD is preventable (paper published 2002)
- ASPVD due to HTN: surgery delayed 4-5 yr (2002)
- Terminal COPD delayed 7 yr (2002)
- WNV (2004)
- Psoriasis (2004)
- Sickle cell: no pain for >6 yr (2007)
ACE = “master”
disease gene
General Architecture of Common Diseases?

Psychiatric diseases

- norepi
- dopamine

AT₁ R
- GRK’s

AT₂ R

Phosphatases

Kinases, e.g. PKC

Insulin R

NIDDM

Cancers

- Cell proliferation
- c-myc
- caspases
- apoptosis

Organ failure

Moskowitz, Diabetes Technology & Therapeutics 4(5), 2002
III. DNA Predictive Diagnostics

- Early, pre-symptomatic diagnosis of 2/3 of cancers in whites is already possible
  - Serial imaging (ultrasound, MRI, blood tests) to detect tumor early
  - Surgical removal of Stage I tumor for a cure

- Goal: lower cancer mortality w/in 3 yr

- Cost: $2.5 M to validate GenoMed’s cancer Healthchip®

- Market: 160 M white Baby-Boomers (USA, EU) @ $500 per assay = $80 B
What’s needed before FDA approval

- Validation genotyping
- Retrospective trials: 3-5 sets of samples, 1000 samples each
- Begin prospective trial w/ my patients
- FDA approval in 3 years
- Collaborate with community and academic cancer centers
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