Peter G. Milner, MD, FACC

Cardiologist and Basic Scientist

December 4, 2007

Peter G. Milner, MD, FACC

- Training: Liverpool University, John Hopkins Hospital, University of Virginia, Washington University
- Assistant Professor Medicine and Genetics, Washington University
- Currently Voluntary Clinical Faculty, Stanford
- 1990: co-founded CV Therapeutics (CVTX)
- 1997: co-founded ARYx Therapeutics (ARYX)

- **Patents**
  - Co-inventor 42 US/EU patents

- **Litigation**
  - 1995 CAFC *In re* Deuel (co-inventor)
    - Attorney: Senninger, Leavitt, Power and Rodell
    - Decision: can obtain protein patent from cDNA sequence
  - 1999 RCJ (UK) Milner vs. Milner Neocal
    - Attorney: Slaughter and May, Justin Turner QC
    - Decision: Fiduciary duty of director to assign Patent is not absolute and is limited by competing obligations

ARYx Therapeutics

The Problem

- Approved drugs have serious safety problems identified post launch
  - 548 NCEs approved from 1975-1999
    - 56 acquired black box warnings or have been taken off the market (JAMA 2002)
- 55% of all drugs are cleared by P450 3A4
  - Potential for drug-drug interactions
    - One of the leading causes of hospitalization and death in the United States
    - Adverse drug reactions (JAMA 1994)

The ARYx Technology Solution

- ARYx's RetroMetabolic Engineering (ARM™)

The ARYx Solution

- Engineers Metabolism for Safety
- Preserves Pharmacology for Efficacy
- Exploits Proven Clinical Pathways
- Generates New Intellectual Property

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Product Pipeline

Address Large Commercial Opportunities

Product	Development Status	Indication
ATI-7505	Phase 2	Multiple GI indications
ATI-5923	Phase 2	Anti-coagulation
ATI-2042	Phase 2	Atrial fibrillation

Triple Threat #1

- Supreme Court
  - *KSR v Teleflex* (2007):
    - 35 USC §103 obviousness bar raised; Teaching Suggestion Motivation (TSM) test deemphasized
  - *Medimmune v Genentech* (2007)
    - Licensee in good standing may file a declaratory judgment action
  - *Ebay v MercExchange* (2006)
    - No longer a near guarantee of injunctive relief against infringers
  - *In re Seagate* (2007)
    - Willful infringement bar raised; likelihood of enhanced damages reduced

Triple Threat #2

- USPTO Rule-Making
  - Presently on hold
    - (Tafas/GSK v Dudas/USPTO)
- Continuation Practice
  - Only two continuations (or CIPs) by right ("showing" for additional continuations onerous)
  - Only one request for Continued Examination (RCE)
- Claim Changes
  - 5 independent, 25 total
  - If more, Examination Support Document (ESD) must be filed
    - AIPLA estimates average cost of ESD at $25K due to claim-by-claim comparison of applicant's claims versus prior art
    - Prior art search results including search criteria
    - Copious on-the-record statements on patentability increase odds of inadvertent inequitable conduct

Triple Threat #2 – Cont'd…

- USPTO Rule-Making (Proposed for 2008)
  - Changes on the horizon:
    - Information Disclosure Statements (IDS)
      - ESD-like document if more than 20 references cited (or any "long" references)
      - USPTO headed toward submission of search results and criteria, and ESD for all applications without exception
    - Claim format (Markush language)
      - Significantly restricted use of pharma's favorite COM claim format
      - Vague standard of examiner review ("must not be difficult to construe") with significant consequences (e.g., no current mechanism to appeal examiner holding of format irregularities)
    - Appeal process – may reduce only remaining means to maximize patent holdings in light of continuation practice changes

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Triple Threat #3

- Legislative Reform

Issue	House (Passed September 7)	Senate (Considered dead this term)
Apportionment of Damages	Reasonable royalty may be calculated from *the economic value attributable to patent's contribution over prior art*	■ Similar to H.R. 1908
Post-Grant Opposition	■ 1st Window: YES; 2nd Window: NO ■ There is no presumption of validity ■ Lower "preponderance of the evidence" standard used versus "clear and convincing" standard in court	■ 1st Window: YES; 2nd Window: YES ■ 2nd Window: must petition within 12 months of notice alleging infringement and showing of likely "significant economic harm"
Disclosure Requirement	■ codifies USPTO's rule-making authority (to require search reports, ESDs, etc.)	■ Similar to H.R. 1908
Venue	■ Includes defendant-based (biased) venue provisions ■ Cannot manufacture venue	■ Similar to H.R. 1908

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- CHI Lobbying Efforts: Against H.R. 1908 and S.1145
  - **April 2007, Washington DC**
    - Meetings with Representatives Bilbray, Woosley, Honda, Drier, Issa, Thompson, Lofgren, Eschoo, Bono; and,
    - Offices of Senator Feinstein and Speaker Pelosi
  - **September 2007, San Diego, CA**: House Republican Conference
    - Representatives Bilbray, Fossella, Issa
  - **October 2007, Washington DC**: CHI, NVCA, MDMA, NMA
    - Meetings with Representative Fossella and offices of Senators Boxer and Kyl
    - Senate staff briefing and press briefing
    - Letter against S.1145 signed by 420 companies

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Issues Raised in Lobbying

- Impact on US Trade and Global Competitiveness
  - Patent harmonization in BRICK countries
  - Knock on effect on trademarks and copyright
- Negative Impact on Job Creation
- Negative Impact on Inventiveness and Medical Product Innovation
- Chilling Effect on Patent Attorneys' Ability to Give Advice to Clients
  - Inequitable conduct
- Cases Cited by Proponents of Legislation Do Not Hold Up under Close Scrutiny
- Adverse Effect on Ability of Entrepreneurs and Small Companies to Raise Venture Financing
  - Lack of Certainty for Venture Capitalists
- Anticompetitive Legislation Favors Big Companies Over Small Companies
  - Reduces ability of innovative new products to break through markets dominated by logos and trademarks controlled by global giants

Focus of Lobbying Efforts

- Against Rule-Making Authority by PTO (as currently proposed by PTO)
- Against Proposed Legislation Giving Rule-Making Authority to PTO
- Limiting Number of Claims and Continuations
- Against Post Grant Review (First and Second "Window"), In Particular Second Window
  - Re-examination process removed from courts and transferred to PTO
  - Legal basis of validity of claims would be reduced
- Against Reduced Ability to Obtain Injunction to Protect Products
- Against Apportionment of Damages
- Limit Mandatory Search Requirements
- Revise or Remove Proposed New Definitions of Inequitable Conduct

Main Recommendation

- In principle not opposed to patent reform that increases the quality and reduces the quantity of patents issued provided that...
  - once issued
    - they are respected;
    - they are presumed valid;
    - they are easily enforced; and,
    - infringers are punished

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