Obstacles to Translation:
Financial Issues
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AGENDA

MPM Capital introduction
Healthcare venture capital drivers/trends
The investment case in rare diseases
Implications for entrepreneurs
MPM CAPITAL HISTORY AND STRATEGY

MPM BioEquities

MPM BV1 $230 million
MPM BV2 $600 million
MPM BV3 $950 million
MPM BV4

MPM founded
Signature transactions: Medigene, Sepracor, TKT, The Medicines Co.

'92 '97 '98 '99 '00 '01 '02 '03 '04 '05 '06

• Healthcare product specialist (drugs + devices)
• Leverage scale for success: $2+ billion under management
• Exploit synergies between private / public investing
• Assembled unrivaled team of 25 investment professionals
• Full spectrum venture capital investing (startup to late-stage)
Healthcare

- 20 - 30% of total VC
- ~$7B / yr
- Today, dominated by specialist firms with $200-600M funds
- Large $ increasingly available for compelling, capital intensive projects (e.g. clinical trials)
WW BIOTECH & MEDICAL DEVICE INVESTING
Where are VC $s going?

Biotech / Med Devices

- 400-500 deals per year
- BioPharma dominates
- US = 75% of $$ and 50% of companies
CURRENT INVESTING ENVIRONMENT

- Early stage platforms and research technology companies extremely challenging to finance privately and publicly
- Clinical stage assets and real products/drugs near exclusive focus of public investors and majority focus of VC
  - Classic financial metrics apply (NPV)
  - Clear path to increase in asset value (clin/reg milestones)
  - Look/feel like the immediate precursor to current mid-pharma and mature biotech companies
  - IPO valuations driven by clinical efficacy (P2+)
TWO TYPES OF PHARMA/BIOTECH PRODUCT OPPORTUNITIES

Niche Areas/Specialty Pharmaceutical companies
  • Smaller revenue opportunities
  • But focused market = addressable with modest salesforce
  • Integrated and independent company possible without need to sell majority economics to Big Pharma

Major Market/Blockbuster companies
  • In major markets, P3/launch exceedingly expensive and challenging
  • P3 and launch are Pharma’s power alley
  • Generate P2 data then share risk and opportunity with Pharma
RARE DISEASE INVESTING
A key feature of current environment

Value Capture

• Company owns entire value chain including sales/marketing for niche market

Grave, unmet medical needs a consistent focus of biotech and of VC

• FDA motivated – clinical and regulatory bar lower = faster + cheaper
• Efficacy is key—totally unblemished safety not required for approval; convenient /cheap QD oral pill not required for market/patient acceptance
• Solutions for real unmet needs yield pricing flexibility (so far)

Proven pathway to success and returns

• Several public companies doing well by doing good, e.g., Biomarin
RARE DISEASE INVESTING
Investment case issues

Value variables are: COST, TIME, RISK, RETURN

Science/medical rationale must be clear

- TIME/COST – Can’t support expensive, lengthy validation + optimization
- LOW RISK - Clinical proof of mechanism required
- BIG PAYOUT - Value of therapy must be large (Survival/QOL) to support premium pricing + adequate revenues on small patient base

Capital efficiency to clinical proof of concept

- Clear, accepted clinical endpoints are essential (reduce regulatory RISK)
- Surrogate endpoints better (often essential to reduce TIME)
- Disease progression must be understood (often poorly characterized) RISK
- Manufacturing issues must not overwhelm COST/RISK (e.g. scale up often very expensive and treacherous)
- Foundation/NIH financial support of clinical trial COST ideal
RARE DISEASE INVESTING
Business case models (wins)

- Genzyme- Cerezyme (Gaucher’s)
- Medimmune- Synagis (mAb for prevention of RSV in LBWT)
- Actelion- Tracleer (PHT and scleroderma)
- United Therapeutics- Remodulin (PHT)
- Geltex/Genzyme- Renagel (hypercalcemia in ESRD)
- Cubist- Cidecin (CSSI in hospital)
- Celgene- Thalomid (Multiple myeloma and leprosy)
- TKT/Shire- Replagal (Fabry)
MPM CAPITAL: PARTIAL LIST OF ORPHAN DISEASE PROGRAMS ACROSS PORTFOLIO

Acorda (Spasticity due to spinal cord injury—4AP and Zanaflex)
BioMarin (Hurler’s Disease—Aldurazyme; MPS VI – Naglazyme; PKU - Phenoptin)
Cellerant (Sickle Cell – CLT-001)
Cotherix (Pulmonary Hypertension--Ventavis)
Intercell (Japanese Encephalitis--IC51vaccine; TB vaccine)
Kalobios (Cystic Fibrosis pseudomonas infections – KB001)
Macrogenics (West Nile vaccine; ITP—anti-CD16)
Peptimmune (Pemphigus vulgaris; PI 2301/RR MS)
Pharmathene (Nerve gas exposure – Protexia; Anthrax – Valortim)
Tercica (Severe primary IGF-1 deficiency -- Increlex)
Verus (Anaphylaxis – TwinJect epinephrine)
Viacell (Cord blood transplant – CB001)
MPM SIGNATURE DEAL: BioMarin

Case at funding

- Highly predictive dog model available
- Grave disease with no options
- Surrogate endpoint of degradation would suffice
- Single pivotal trial would suffice for regulatory approval
- Value inflection point at entry into man
- “Genzyme” business model available

MPM Role

Introduce and shape critical partnership (Genzyme)

Lead investor

Office of president

Successes/Challenges

- Early IPO achieved
- Strong partnership sustained company
- Significant advance for patients achieved
- FDA demanded clinical benefit be proven in duplicate; surrogate inadequate
- Manufacturing issues: expensive biologic
SUMMARY

For a niche company addressing a small (by patient numbers) opportunity:

- Great people
  - Experienced entrepreneurs with knowledge of the specialty area: science, medicine, marketing, or all three
- Clear biologic rationale
  - Low science risk
- Clear and quick/inexpensive clinical/regulatory path
  - Orphan Drug designation desirable
  - Surrogate trial endpoints exist and accepted by FDA
- Clear market opportunity
  - Reimbursement strategy (clinical value)
  - Lack of therapeutic alternatives/competition
  - Patients available/identifiable
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LATE-STAGE PRODUCTS KEY TO IPO VALUE

Biotech IPOs Relative to Stage of Development

- Pre Bubble IPOs
- Post Bubble IPOs
- Pre Bubble valuation
- Post Bubble valuation

Data does not include ‘99-'00 “Bubble” period