



Drug Delivery Systems

Photocure Capital Markets Day

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www.novasecta.com

NovaSecta specializes in smaller to medium-sized pharmaceutical companies ('MidPharmas')

- ❖ **We are uniquely knowledgeable and connected in the MidPharma sector.**
- ❖ **We originate and manage collaborations and programs for MidPharmas, and provide customized support for their initiatives and projects.**
- ❖ **We support MidPharmas' activities in Corporate Development and R&D.**

Today's successful Drug Delivery Companies are all MidPharmas

My message today

- ❖ **The pharmaceutical industry needs new models in drug development.**
- ❖ **Drug Delivery companies and technologies form part of the solution ...**
- ❖ **... And have real value that can be monetized effectively.**

***The Need for New Models in
Drug Development***

Investors are no longer confident that Big Pharmas will create value

- ❖ For the old “big three”, share prices are similar to 10 years ago.

Pfizer



GSK

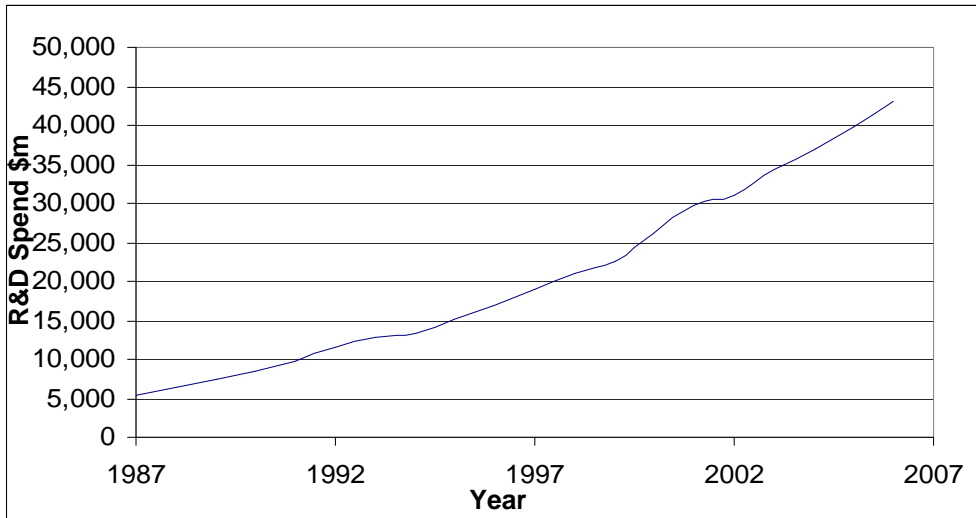


Merck



Source: FT.com

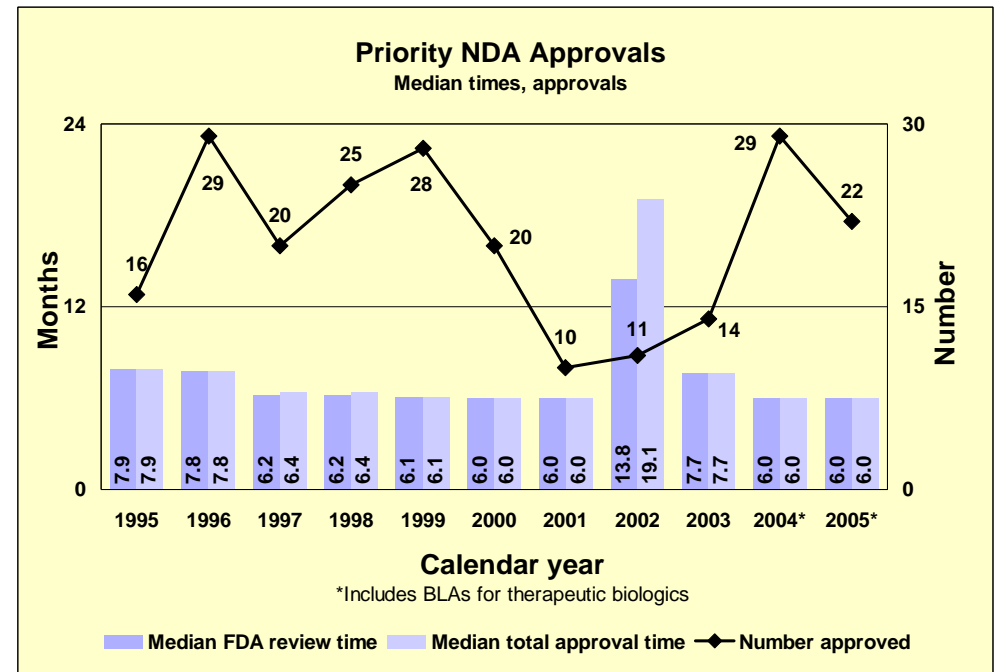
And the pharmaceutical industry has a serious R&D productivity problem



Source: PhRMA Pharmaceutical Industry Profile 2007

More R&D money spent ...

... for similar annual output.



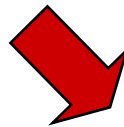
Source: CDER 2005 Report to the Nation

***Drug Delivery:
Part of the Solution***

“Drug Delivery” (DD) comprises a wide diversity of technologies and approaches for creating better drugs

❖ Several alternative routes of administration, e.g. :

- Oral
- Inhaled
- Injectable
- Intranasal
- Topical
- Etc.



❖ ... and many types of DD technology, e.g. :

- Formulation and Galenics
- Inhalation and Respiratory Delivery
- Injectable Controlled Release
- Needleless Injection
- Oral Controlled
- Patches
- Pegylation
- Polymers and Lipids
- Protein Delivery
- Release and Bioavailability
- Transdermal
- Solubilization

Drug Delivery therefore offers one way to deal with the Pharmaceutical industry's ills

- ❖ **Differentiate by adding a layer of IP to an off-patent or nearly patent-expired product:**
 - Create effective Life Cycle Management (LCM).
 - Combat increased generic competition.

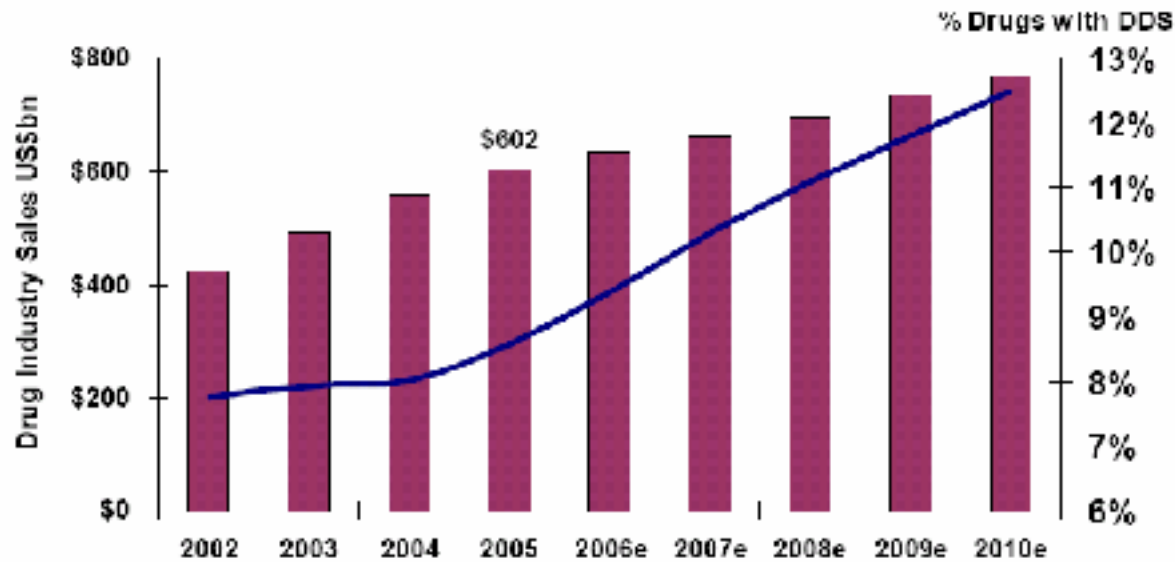
- ❖ **Fast-track products to market based on “safe” well-known molecules:**
 - Combat increased difficulty in achieving “new” product launches.
 - Lower the attrition rates in clinical development.
 - Alleviate regulatory concerns over drug safety
 -

- ❖ **Take advantage of favourable product development economics:**
 - Develop “drug delivery” products with 2-6 years research and \$2m-\$100m cost:
 - Compares with 10-15 years research and \$800m-\$1.7bn for major pharma new chemical entity.

- ❖ **Create “quantum leap” solutions for novel protein-based treatments:**
 - Open up new therapeutic possibilities by enabling cell entry by novel biotech molecules.
 - Introduce new paradigms for therapy (monoclonal antibodies analogy).

DD drugs sales are expected to top \$90bn by 2010 as they continue to increase in share of the global pharmaceutical market

Figure 1 – Global Pharmaceutical Market & Drug Delivery Drugs Sales US\$b



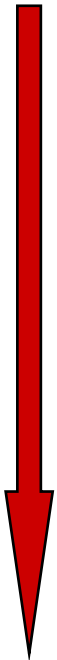
Source: IMS Health

Drug Delivery is now an established and growing industry in its own right

- ❖ **The pioneer in the industry, ALZA Corporation was founded by Dr. Alejandro Zaffaroni in 1968 to realize his vision of “*sophisticated pharmaceutical products that precisely control the targeting, timing and dosing of therapeutic compounds*”:**
 - ALZA was subsequently sold to J&J in 2001 for \$10.5bn, and still thrives as a business unit.
- ❖ **There are now at least 60 listed drug delivery companies world-wide, and a similar number of established private companies.**
- ❖ **Drug Delivery companies have created value for their owners as they have evolved from technology platform out-licensors to fully integrated Specialty Pharmaceutical companies.**

Drug Delivery companies have typically evolved over time from platform technology exploitation to profitable specialty pharmaceutical company

DD Company Archetype	Income Sources	Valuation Basis	Examples
Platform Technology	Service Revenue or Seed / VC Funding	Technology Potential	Access Pharmaceuticals AP Pharma Sontra Medical
Technology Licensor	Milestone Payments for Compounds	Pipeline Potential Expected Deal Income	Penwest Pharmaceuticals Inovio Biomedical Flamel Technologies Inc
Product Developer	Milestones and Royalties Some Sales	Pipeline Potential Revenue Growth	Nektar Therapeutics Alkermes QLT
Specialty Pharma	Product Sales	EBITDA and Other Multiples	Biovail KV Pharmaceutical Enzon



Successful Drug Delivery Companies can mix these models as they grow

The more established drug delivery companies are therefore now following either a “product developer” or a “specialty pharma” model ...

Selected Drug Delivery Companies in Two Segments, Each Ranked by Market Capitalisation*

	Company Name	Country	Company Type	MktCap \$m	Revenue \$m	R&D \$m	R&D % Rev
“Specialty Pharma”	Biovail Corp	Canada	Pharma - controlled release	3,939	1,068	95	9%
	KV Pharmaceutical Company	USA	Specialty pharma	1,000	368	29	8%
	Noven Pharmaceuticals Inc	USA	DD systems - transdermal	580	61	11	19%
	Enzon Inc	USA	Pharma - platform based	375	186	44	23%
	Bradley Pharmaceuticals Inc	USA	Pharma - Rx and OTC	368	145	10	7%
	Vivus Inc	USA	Pharma - TA focused	315	14	2	15%
	Bentley Pharmaceuticals Inc	USA	DD - absorption technologies	269	109	10	10%
“Product Developer”	Alkermes Inc	USA	Pharma - DD	1,720	167	88	53%
	Nektar Therapeutics	USA	DD solutions	1,067	218	149	69%
	Flamel Technologies Inc	France	Pharma - platform based	677	23	47	206%
	QLT	Canada	Pharma - TA focused	577	175	56	32%
	Vectura Ltd	UK	DD - pulmonary	538	22	31	141%
	Labopharm Inc	Canada	Pharma - based on controlled release	361	15	17	113%
	Nastech Pharmaceutical Company Inc	USA	DD - nasal	312	9	12	130%
	Penwest Pharmaceuticals Company	USA	Developer - DD technologies	305	3	23	653%
	Inovio Biomedical	USA	Biopharma - technology-based	167	3	9	245%
	Acrux Ltd	Australia	DD systems - transdermal	161	2	4	200%
	Nexmed Inc	USA	Pharma - platform based	139	2	5	291%
	Columbia Laboratories Inc	USA	Pharma - TA based	132	17	7	38%

* Market Capitalisation at 30May07; most recent annual reported revenue and R&D spend (typically 2006)

... and have typically built up two or more technology platforms to expand reach and diversify risk

❖ **Alkermes (2):**

- Injectable Extended-Release technology and Pulmonary Drug Delivery technology.

❖ **Flamel Technologies (2):**

- Medusa[®], a self-assembled poly-aminoacid nanoparticles system, and Micropump[®] platform which enables the controlled delivery of small molecule drugs that are best absorbed in the small intestine.

❖ **Nektar Therapeutics (2):**

- Advanced PEGylation Technology and Advanced Pulmonary Delivery.

❖ **PenWest Pharmaceuticals (3):**

- From the TIMERx[®], platform, developed two additional and distinct oral drug delivery systems: Geminex[®] and SyncroDose[™].

❖ **QLT (3):**

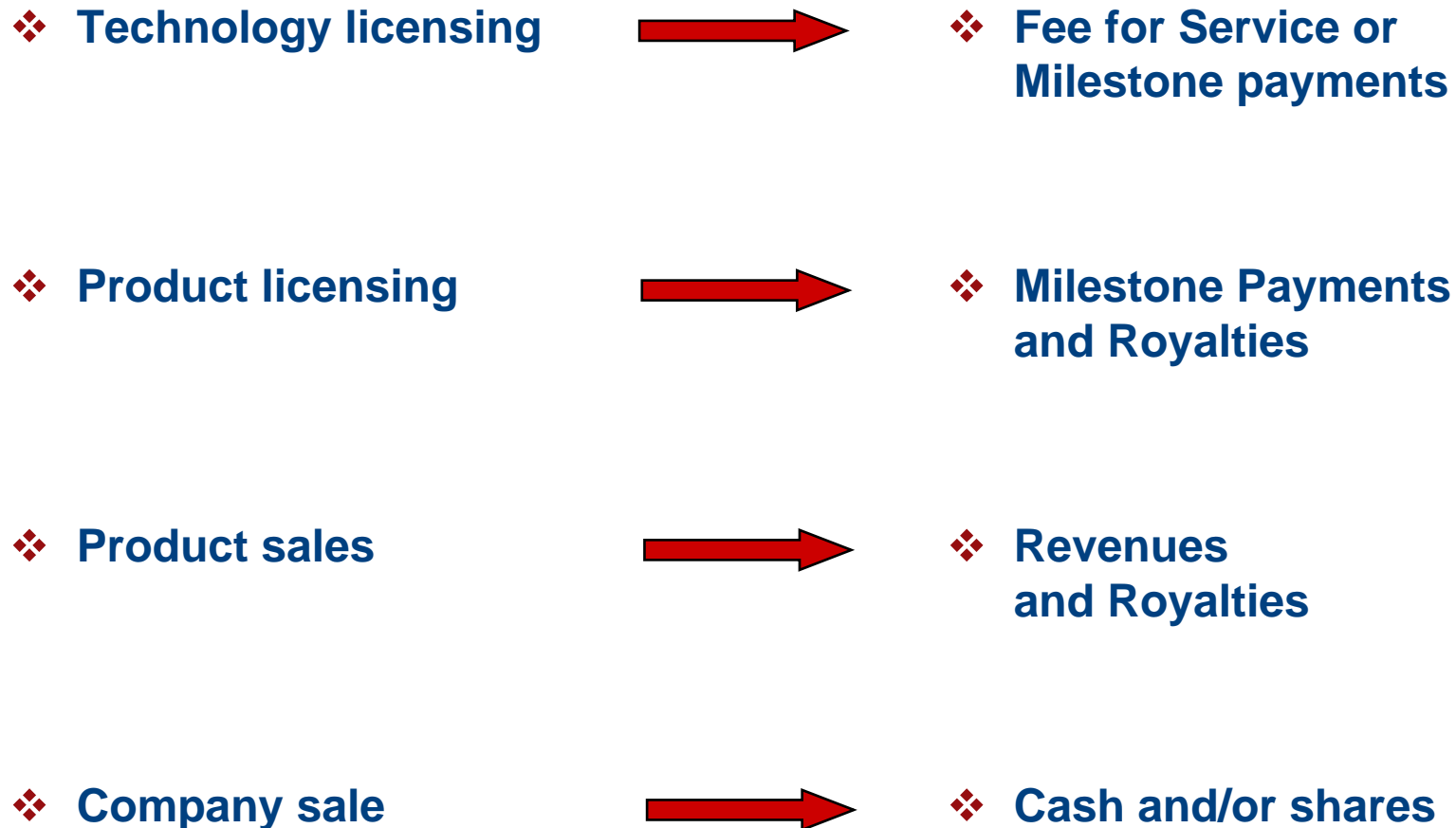
- Photodynamic Therapy, Atrigel[®] Drug Delivery, Solvent Microparticle System[™]

❖ **KV Pharmaceutical (4):**

- 15 technologies, falling within four principal areas: 1) SITE RELEASE[®] (bio-adhesive), 2) Tastemasking, 3) Quick-Dissolving Tablets, and 4) Oral Extended/Delayed Release.

***Monetizing the Value
of Drug Delivery***

Drug Delivery companies have applied several approaches to monetizing the value of their technologies



Drug Delivery companies technologies have enabled major product development deals

❖ Pfizer/Eyetech \$295m deal was enabled by Enzon-Nektar pegylation of Macugen

- Eyetech receives from Pfizer \$75m cash upfront, \$25m equity purchase, up to \$195m in approval milestones
- Milestones, manufacturing rights to the PEG derivative, royalties and manufacturing revenues between 2.5-7.5%

❖ Lilly/Amylin \$435m deal on Exenatide was enabled by Alkermes technology

- Amylin gets up to \$435m from Lilly - \$80m upfront, with profit split, co-promotion
- Key milestones are formulation/approval of extended-release version via Alkermes' Medisorb technology.
- Amylin pays Alkermes:
 - \$625k milestone once feasibility work accepted
 - Additional regulatory and commercial milestones
 - Royalties & manufacturing payments
 - Warrants to buy 75,000 Amylin shares for \$10.55/sh (then price: \$21.32)

Drug Delivery companies have also monetized their assets through product licensing deals

- ❖ **Alpharma entered into an exclusive licensing agreement with Tris Pharma, a company engaged in drug development technologies.**
 - Alpharma will pay \$15m in milestone payments + additional clinical development expenses.
 - The agreement also calls for royalty payments of net sales.
- ❖ **Vivus agreed to transfer exclusive rights to their metered dose transdermal oestradiol spray to KV Pharmaceutical.**
 - Vivus will receive an up-front payment of \$10mill upon closing and additional \$140mill upon NDA approval.
 - The company could also receive royalty payments up to \$30mill based on sales.
- ❖ **Adams Respiratory Therapeutics has entered into a license and collaboration agreement with MonoSolRx, a privately held DDS company that uses edible film as a fast dissolve oral drug delivery platform to develop mainly OTC products.**
 - The exact value of the deal is yet unknown but expected to be >\$100mill in total.

As well as monetizing value by ongoing own-product sales, DD companies can and do monetize their value by being acquired

Selected Drug Delivery Company Acquisitions

Acquired Company	Technology	Acquirer	Year	Price \$m
Alza	Multiple	J&J	1991	10,500
CIMA Labs	Fast-dissolve	Cephalon	2003	515
Alaris Infusion	IV products	Cardinal	2004	2,100
Atrix	Cancer, skin products	QLT	2004	885
Andrx	Oral controlled release	Watson	2006	1,900
Connetics	Multiple	Stiefel	2006	640
Innovata	Inhaler	Vectura	2006	243
Kos	Metered dose	Abbott	2006	3,700

Acquirers are typically specialist MidPharmas

Conclusion: My message today

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