

NACDS

pharmacy & 2011 technology conference

August 27 - 30, 2011 ■ Boston Convention & Exhibition Center ■ Boston, MA

- Date:** Tuesday, August 30, 2011
- Time:** 9:45 a.m. – 10:45 a.m.
- Location:** Boston Convention & Exhibition Center, Meeting Level 2, Room 258 AB
- Title:** **The Pharmaceutical Pipeline - A View Into the Future**
ACPE # 0206-0000-11-520-L04-P (0.1 CEU)
- Speaker:** Brian W. Kolling, PharmD, OptumRx
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Learning Objectives:

At the conclusion of this knowledge-based program, participants will be better able to:

- Identify drugs that will be driving pharmacy trends in the future
- Explain the effect that biosimilars will have on the specialty market
- Identify upcoming generics and the impact they will have on retail pharmacy

Don't forget to obtain continuing education credit for your participation in this session. Instructions for processing your statement of credit online are included in your registration bag.



The Pharmaceutical Pipeline: A View Into the Future

Brian W. Kolling, Pharm.D.
Senior Director, Pipeline & Trend Forecasting, Part D
August 30, 2011

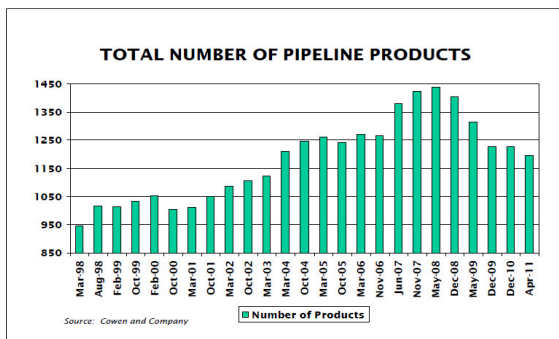
Discussion Points

- The "State of the Pipeline"
- Top Developments of 2011
- Therapeutic Category Review
 - 2011 Approvals
 - On the Horizon
 - Generics



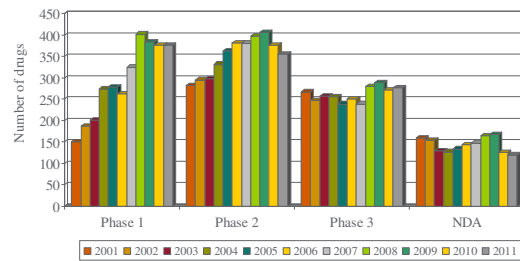
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Overall Pipeline Activity Declining



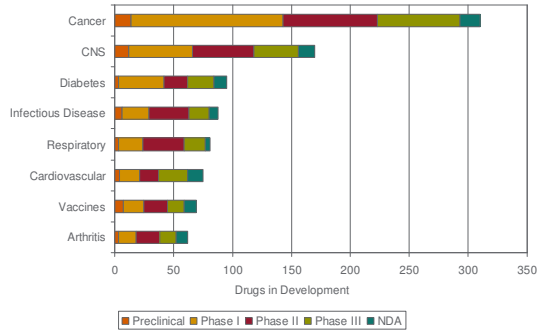
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Pipeline - Phase Of Research

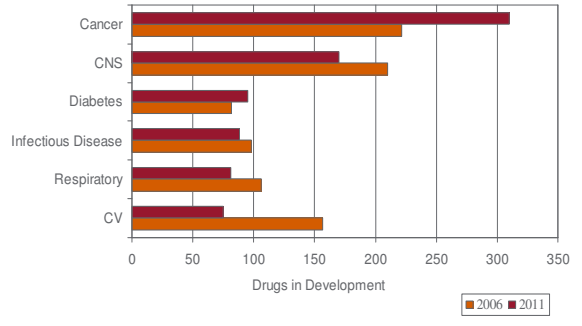


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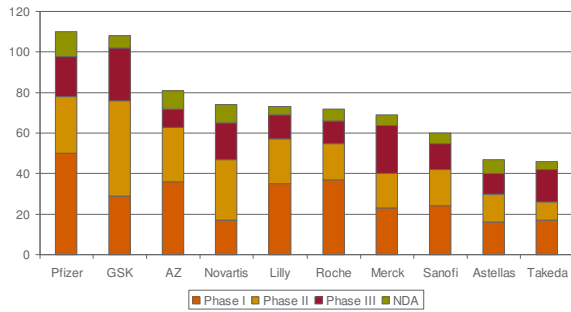
Pipeline by Disease State



Pipeline Comparison: 2011 to 2006



Who Has the Biggest Pipelines?



R&D – Where Are We Headed?

- New drug approvals have not kept pace with R&D spend
- The "patent cliff" has resulted in fundamental changes to research on new drugs
- Higher barrier to entry means more investment, yet most money today is spent in Phase II or earlier, which has highest failure rate

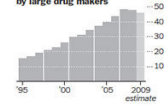
Solutions?

- In-license pipeline products later in development and leave early development work to partner company
- Share development risk with a similar-size company
- Shift to "friendlier" market (i.e. specialty, emerging markets, animal health)
- Exit selected markets

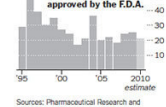
Fewer New Drugs

Large drug makers have begun to reduce spending on research and development, while the industry's output of new drugs approved by the Food and Drug Administration remains in decline.

Research spending by large drug makers



New pharmaceuticals approved by the F.D.A.



Sources: Pharmaceutical Research and Manufacturers of America; F.D.A.

THE NEW YORK TIMES

Two Approaches to address lagging R&D

January 22, 2011

Federal Research Center Will Help Develop Medicines

By GARDNER HARRIS

The Obama administration has become so concerned about the slowing pace of new drugs coming out of the pharmaceutical industry that officials have decided to start a billion-dollar government drug development center to help create medicines.

February 9, 2011

New Chief Revises Goals and Spending for Pfizer

By DUFF WILSON

Pfizer, the drug maker, announced plans Tuesday to slash its research spending by as much as \$2.9 billion in the next two years, including closing the English labs that invented Viagra.



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Drug Approvals in 2011 – YTD New Molecular Entities

Drug	Manufacturer	Indication	Approval Date
Dificid	Optimer	Treatment of <i>C. difficile</i> diarrhea	May 27
Incivek	Vertex	Hepatitis C	May 23
Edurant	Tibotec	HIV	May 20
Victrelis	Merck	Hepatitis C	May 13
Tradjenta	Boehringer Ingelheim	Type 2 diabetes	May 2
Zytiga	J&J	Metastatic prostate cancer	April 28
vandetanib	AstraZeneca	Advanced medullary thyroid cancer	April 6
Horizant	GSK	Restless legs syndrome	April 6
Yervoy	BMS	Malignant myeloma	March 25
Benlysta	GSK	Lupus	March 9
Daliresp	Forest	Add-on for severe COPD	March 1
Edarbi	Takeda	Hypertension	February 25
Vilbyrd	Forest	Depression	January 21
Natroba	Parapro	Head lice	January 18



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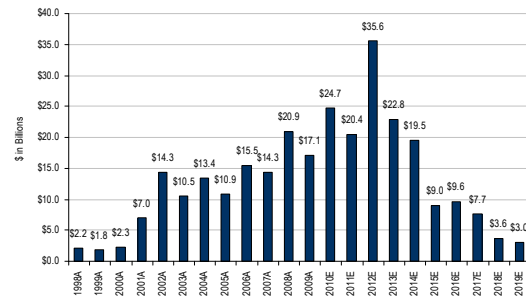
First-Time Generics in 2011

Drug	Manufacturer	Generic	Annual sales (US)
Vfend	Pfizer	February 15	\$260 million
Xalatan	Pfizer	March 22	\$626 million
Femara	Novartis	April 22	\$669 million
Concerta	J&J	May 1	\$1.4 billion
Levaquin	J&J	June 20	\$1.5 billion
Uroxatral	sanofi-aventis	July 18	\$249 million
Zyprexa	Lilly	October 23	\$2.5 billion
Caduet	Pfizer	November 30	\$339 million
Lipitor	Pfizer	November 30	\$5.3 billion



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Generic Opportunity Still Significant



Source: FDA Orange Book, SEC Filings, IMS Health, USPTO, & BuA/Merrill Lynch Global Research



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Top Developments to Watch - 2011

1. Zyprexa and Lipitor generics
2. Approval and launch of telaprevir and/or boceprevir
3. The clinical development of vorapaxar
4. Additional Phase III results for tofacitinib
5. Approval and launch of Benlysta



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Cardiovascular Pipeline – 2011 Approvals

Brilinta (ticagrelor) – AstraZeneca

- Reversible ADP receptor blocker
- Proposed indication: Acute coronary syndrome
- Approved July 20

Xarelto (rivaroxaban) - Bayer/J&J

- First-in-class Factor Xa inhibitor
- Proposed indication: prophylaxis of DVT and PE in patients undergoing hip or knee replacement surgery
- Approved July 1



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Cardiovascular Pipeline – On the Horizon

Eliquis (apixiban) – BMS/Pfizer

- Factor Xa inhibitor for stroke prevention in atrial fibrillation and VTE prevention and treatment
- AVERROES trial vs. aspirin stopped early due to clinical benefit seen with apixaban; ARISTOTLE study will compare Apixiban to warfarin and should report mid-2011
- NDA filing after ARISTOTLE results released

Edoxaban – Daiichi-Sankyo

- Factor Xa inhibitor for atrial fibrillation and VTE
- Phase III results vs. enoxaparin in VTE prevention were generally positive; results vs. warfarin in AF expected in 2012
- US filing strategy not disclosed



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Cardiovascular Pipeline – On the Horizon

Lomitapide – Aegerion

- Oral MTP-I inhibitor for homozygous familial hypercholesterolemia
- MTP-I prevents assembly and limits release of lipoproteins
- LDL and TG reductions of 50%
- NDA filing by end of 2011; orphan drug status

AMR101 – Amarin

- Oral therapy for the treatment of elevated triglycerides and mixed dyslipidemia
- Single active ingredient (ethyl icosapentate)
- MARINE and ANCHOR trials show decrease in triglycerides with little impact on LDL
- NDA filing expected 3Q 2011



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Cardiovascular Pipeline – On the Horizon

MK-0524A – Merck

- Niacin plus laropiprant (anti-flushing agent) for treatment of primary hypercholesterolemia
- MK-0524B adds simvastatin
- Refiling for MK-0524A expected in 2012; followed by 0524B filing

Dalcetrapib – Roche

- CETP inhibitor for the treatment of dyslipidemia
- Phase IIb/III plaque and endothelial data expected in 2011; Outcomes study may report interim data as well
- Path to approval is likely complicated, given past experience in class
- NDA filing in 2013



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Cardiovascular Pipeline - Generics

Drug	Manufacturer	Generic launch	Additional info
Tricor	Abbott	March 2011-July 2012	Settlement; launch likely 7/1/12
Lipitor	Pfizer	November 2011	Settlement
Avapro	BMS	March 2012	
Plavix	BMS	May 2012	
Atacand	AstraZeneca	December 2012	
Diovan	Novartis	September 2012	
Niaspan	Abbott	September 2013	Settlement
Crestor	AstraZeneca	July 2016	Recent court ruling could extend to 2018



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CNS Pipeline – 2011 Approvals

Remoxy (oxycodone) – Pfizer

- Twice-daily formulation for treatment of chronic pain
- Contains ORADUR gel cap technology – less prone to abuse?
- PDUFA 6/23/11; “Complete Response” letter issued

Zelrix (sumatriptan) – Nupathe

- Transdermal sumatriptan for treatment of acute migraine
- Single-use patch; controlled delivery over 4 hours via iontophoresis
- PDUFA 8/29/11



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CNS Pipeline – On the Horizon

Cariprazine (RGH-188) – Forest

- Atypical antipsychotic for treatment of schizophrenia and bipolar mania
- Mechanism similar to Abilify, but potential for improved safety profile
- Phase III results expected 2nd half 2011

TC-5214 – Targacept/AstraZeneca

- Nicotinic ion channel blocker for major depressive disorder
- Developed as adjunct to first-line antidepressants
- Phase III began 2H10; NDA filing in 2012



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CNS Pipeline – On the Horizon

Levomilnacipran – *Forest*

- SNRI for treatment of depression; isomer of Savella
- Greater potency and selectivity for NE receptor compared to other SNRIs
- First Phase III trial failed, others ongoing



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CNS Pipeline - Generics

Drug	Manufacturer	Generic launch	Additional info
Zyprexa	Lilly	October 2011	
Lexapro	Forest	March 2012	Multiple generics (2 plus auth)
Seroquel	AstraZeneca	March 2012	Multiple generics
Provigil	Cephalon	April 2012	Settlements
Geodon	Pfizer	September 2012	Multiple generics possible
Lunesta	Sepracor	May 2014	Settlements
Cymbalta	Lilly	July 2014	Multiple generics possible
Abilify	BMS	April 2015	



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Respiratory Pipeline – 2011 Approvals

Arcapta (indacaterol) – *Novartis*

- Once-daily beta agonist inhaler developed as monotherapy for COPD and combination therapy for asthma
- FDA AdCom recommended approval of low-dose but felt high-dose was no more efficacious
- Combination with Asmanex and NVA237 (LAMA) to follow
- Approved July 1



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Respiratory Pipeline – On the Horizon

Ekliira (aclinium) – *Almirall/Forest*

- Twice-daily muscarinic antagonist (LAMA) inhaler for COPD
- Monotherapy and combination inhaler with formoterol in development
- NDA for monotherapy expected in 2011

Glycopyrronium (NVA237) – *Novartis*

- Inhaled long-acting muscarinic antagonist for the treatment of COPD
- Early data suggest similar efficacy to Spiriva
- Combination inhaler with Arcapta in development
- Phase III results expected 2q11 with filing soon after



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Respiratory Pipeline – On the Horizon

Relovair (fluticasone furoate/vilanterol) – GSK

- Once-daily inhaler for COPD and asthma
- Clinical trials suggest modest FEV1 improvements over Advair
- LABA onset of action within minutes
- Phase III results 2H11

GSK573719/vilanterol – Theravance/GSK

Spiriva/olodaterol – Boehringer Ingelheim

QVA149 – Novartis

- Combination LAMA/LABA inhalers for COPD
- All in Phase III or starting Phase III in 2011



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Diabetes Pipeline – 2011 Approvals

Dapagliflozin - BMS/Astra-Zeneca

- Oral sodium glucose co-transporter-2 (SGLT-2) inhibitor – suppresses glucose re-absorption and increases glucose excretion
- Reductions in body weight and blood pressure seen in clinical trials
- Urinary tract and genital infections are primary side effect; drug-induced liver toxicity?
- PDUFA: 10/28/11; Advisory committee voted 9-6 against approval



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Diabetes Pipeline – On the Horizon

Bydureon – exenatide once-weekly (Amylin)

- GLP-1 analog
- Recent DURATION-6 trial failed to demonstrate non-inferiority to Victoza (A1C reduction 1.3% for Bydureon, 1.5% for Victoza)
- CRL issued Oct 2010; FDA requested a thorough QTc study
- NDA re-filed July 2011; six month review expected

Atrezza (inhaled insulin) – MannKind

- Ultra rapid acting insulin that mimics meal-related early insulin release
- Phase III trial demonstrated non-inferiority to Novolog, additional trials in combination with Lantus was also non-inferior, but less weight gain than with premixed insulin + Lantus
- CRL issued Jan 2011; two new trials required



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Diabetes Pipeline – On the Horizon

Albiglutide – GSK

LY2189265 – Lilly

- GLP-1 analogues fused to human albumin
- Weekly dosing
- Phase III; data not expected until 2012

Lixisenatide – sanofi-aventis

- Daily GLP-1 analogue
- Phase III top-line data vs. exenatide suggest non-inferiority but fewer hypoglycemic events
- NDA filing 2012



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Diabetes Pipeline – On the Horizon

Degludec – *Novo Nordisk*

- Long-acting basal insulin
- Phase III data vs. Lantus indicate lower fasting glucose level with degludec, and a trend toward lower nocturnal hypoglycemia
- Phase III for Degludec/Victoza combo expected to begin in 2011
- NDA by end of 2011

Aleglitazar – *Roche*

- PPAR co-agonist for treatment of Type 2 diabetes after a CV event
- Dual effect on glucose and lipid control
- Phase III began February 2010; NDA 2012+



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Diabetes Pipeline - Generics

Drug	Manufacturer	Generic launch	Additional info
Avandia	GSK	March 2012	Teva exclusive
Actos	Takeda	August 2012	Settlement with multiple companies



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Gastrointestinal Pipeline

Linacotide – *Forest*

- Oral guanylate cyclase receptor agonist for chronic constipation and irritable bowel syndrome with constipation
- Acts locally in the gut; no systemic exposure
- Efficacy in abdominal pain may provide marketing advantage
- NDA expected 3Q 2011

Budesonide MMX – *Santarus*

- Oral controlled-release budesonide for the induction of remission of mild or moderate active ulcerative colitis
- Designed to release drug throughout the colon
- NDA expected by end of 2011



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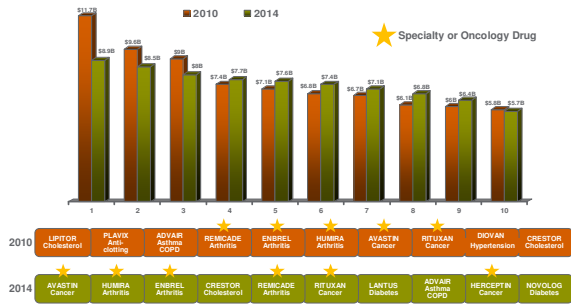
Additional Patent Expirations

Drug	Manufacturer	Generic launch	Additional info
Boniva	Genentech	March 2012	2.5 mg only
Revatio	Pfizer	September 2012	No exclusivity
Aciphex	Eisai/J&J	May 2013	Settlement
Nexium	AstraZeneca	April 2014	
Actonel	Warner Chilcott	June 2014	35 mg only



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Specialty Drugs – A Shifting Market



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Specialty Drugs – Rheumatoid Arthritis

Tofacitinib – Pfizer

- Oral JAK1 and JAK3 inhibitor for the treatment of rheumatoid arthritis
- JAK inhibition suppresses multiple immune response pathways
- Renal, hepatic, and CV side effects may require monitoring
- Phase III results announced throughout 2011; filing later this year

Fostamatinib – AstraZeneca

- Oral SYK (spleen tyrosine kinase) inhibitor
- SYK inhibition blocks signaling of immune cells responsible for the destruction of cartilage and bone
- NDA filing in 2013



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Specialty Drugs – Multiple Sclerosis

Laquinamod – Teva

- Oral, once-daily therapy
- "Unclear how it works exactly, but it does something good"
- First Phase III released in 2010; BRAVO trial vs. Avonex TBR in 2011

Teriflumomide – sanofi-aventis

- Oral, once-daily therapy
- Metabolite of leflunomide; teratogenicity is a concern
- First Phase III released in 2010; TERENE trial vs. Rebif TBR in 2011

BG-12 – Biogen/dec

- Oral, twice daily therapy
- Phase III DEFINE study suggests similar efficacy to Gilenya
- NDA filing possible late 2011/early 2012



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Questions?

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