

Innovation in Biotech/Pharma Industry

Creative Science, Creative Technology,
Creative Niche Product, Creative Uses,
Creative Disease, Creative Regulatory Process,
Creative Business Model, and a Lot More...

Innovation in a Changing IP World

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Keith Chan, Ph.D. 陳桂恒博士

Cornerstone IP Foundation, Taiwan 磐安智財基金會

National Chengchi University, Taiwan 政大 商學院 科管智財所

National Yang Ming University, Taiwan 陽明 生藥所 新藥研究所

E-mail: kchan@globoasia.com

Outline



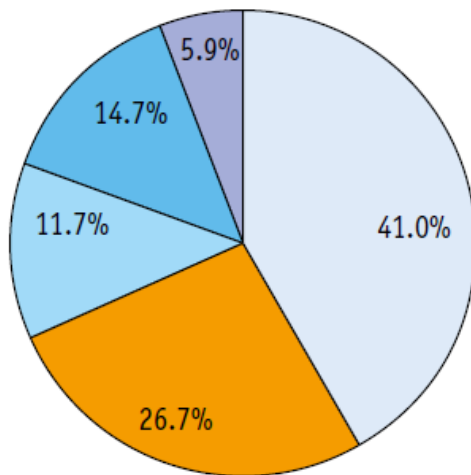
- Innovation Process: Problem–Solution–IP-Execution Paradigm
- Knowledge-Based Economy, Market-Driven, Open Innovation and Biotech/pharma Product Lifecycle Management
- Innovations in Biotech/Pharma Industry
 - ✓ Regulation - Creative regulatory process to speed up drug approval...
 - ✓ Science/Technology - Creative science, technology, application, niche product to meet unmet needs...
 - ✓ Business - Creative uses, creative disease, creative M&S to increase profitability...
 - ✓ Law/IP - Innovative IP process, creative use of Exclusivity and Litigation to secure market share and ensure product longevity...
- Summary - Innovation has no limitation

Why US? Breakdown of World Pharmaceutical Market

2012 Sales

- US biotech/pharma market is the biggest market in the world [with the most predictable, non-discriminatory, transparent, rewarding, world-recognized most advanced drug approval environment]

BREAKDOWN OF THE WORLD PHARMACEUTICAL MARKET – 2012 SALES



Sales of New Medicines Launched during 2007-2011:
62% in US Market v 18% with EU Market

□ North America (USA, Canada)

■ Europe

■ Japan

■ Africa, Asia (excluding Japan) & Australia

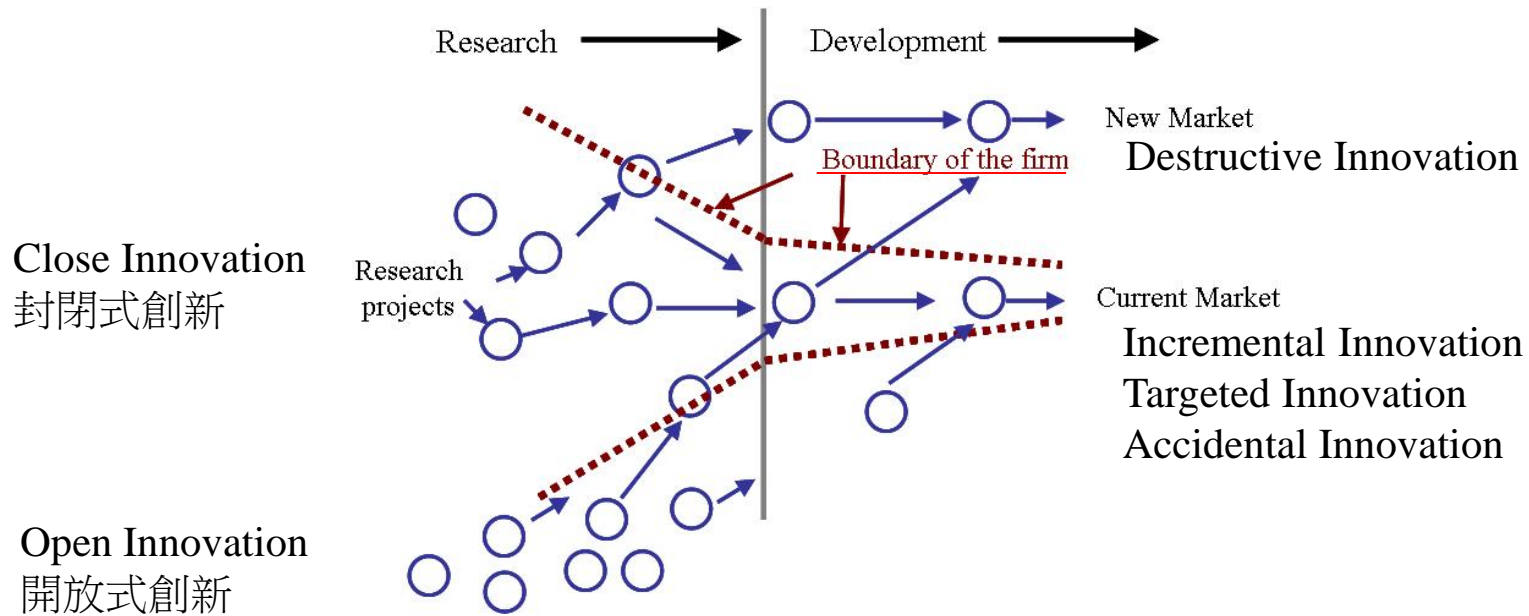
■ Latin America

Estimated Taiwan market = app. 0.6% of the World

Note: Europe includes Turkey and Russia

Source: IMS MIDAS, 2013 (data relate to the 2012 audited global retail pharmaceutical market at ex-factory prices)

Continuum of Innovation



Research and
Discovery

- New processes
- New tools
- Fundamental knowledge

Invention

- Protection of ideas
- Practical application of fundamental knowledge

Innovation

- Product concepts
- Customer needs

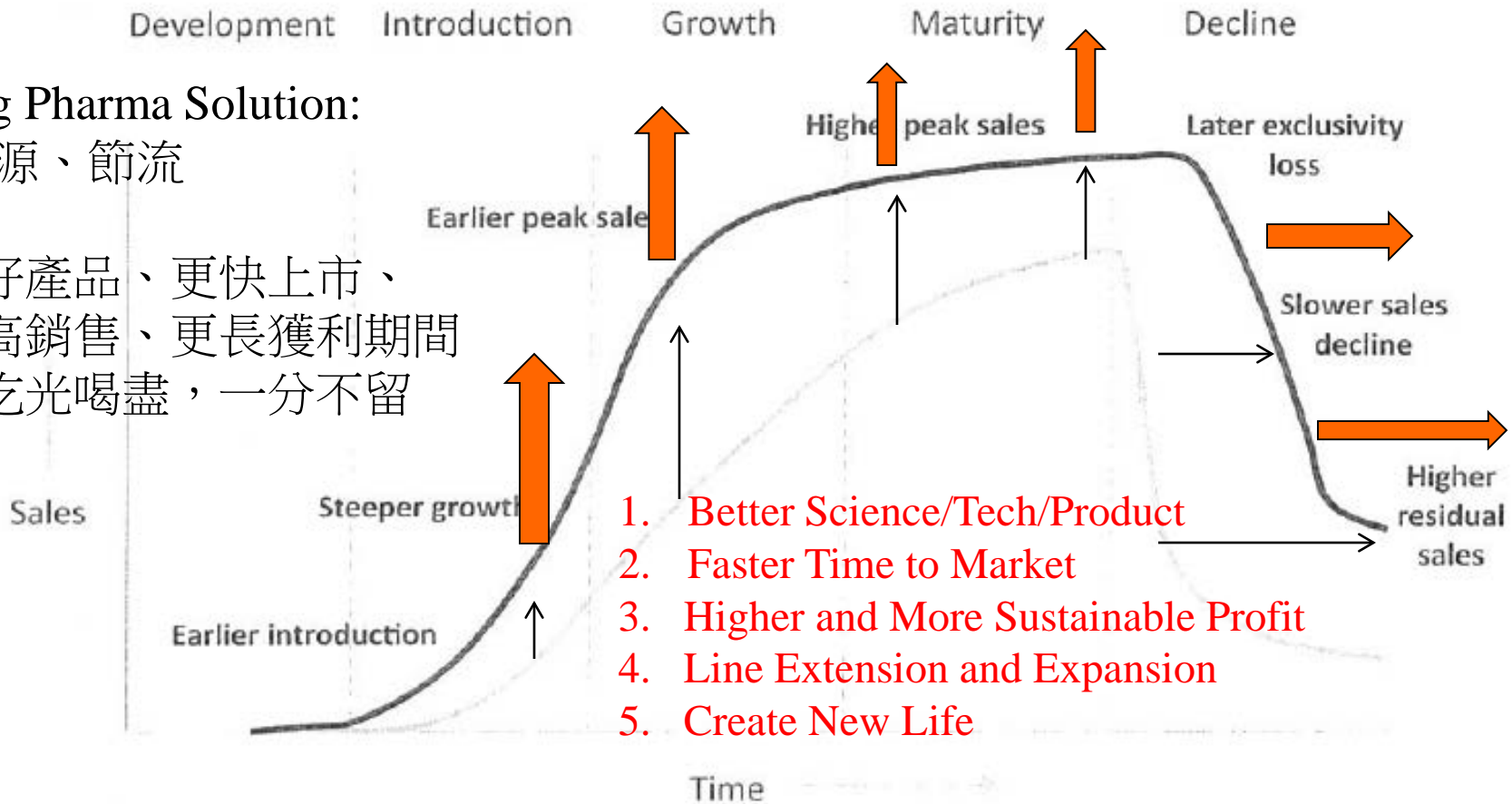
Commercialization

- Product development
- Testing
- Manufacturing
- Distribution channels

Innovation in Lifecycle Management (LCM) on Typical Pharma Product

Big Pharma Solution:
開源、節流

更好產品、更快上市、
更高銷售、更長獲利期間
，吃光喝盡，一分不留



Anyone Who Can Contribute to the LCM is a Welcome Player

Don't Limit Yourself to New Drugs and Earth-Shaking Sciences

- Pioneer → Fellow-On; 2nd in Class, me-too, me-better...
[505(b)(2)*] → Generic Drug [It is a game for everyone]
- Big company is getting bigger and small company must be smarter and faster to survive or win
- Any problem solver, innovator, rainmaker who can help to create value in any form at any stage for any product or set barrier for others is a welcome player [Please don't limit yourself to only new drugs or earth-shaking sciences]
- There is no line between pioneer firm or generic firm [There are no forever friend or forever enemy; only forever money to be made 商場如海、善泳者勝、懂規矩者贏 (搶食世界)]
- *505(b)(2) -第二類新藥 (包括舊藥新用、新投藥途徑、新劑型、同機轉衍生物、me-too、me-better...)

Innovation Has No Boundary in LCM Especially in Biotech/Pharma Industry

- Innovation in every step – from concept to market
[True innovation must be truly protected and utilized]
- Protection/IP/Enforcement - 利用創新/保護、攻城略地、造反有理、寸土不讓。保護 - 工欲善其事，必先利其器。牙簽不能當槍用、但假槍也可以嚇死人 [小心上得山多終遇虎，將軍難免陣中亡]。
 - ✓ Government/Regulation – Better economic and political environment, better regulatory process
 - ✓ Science/Technology - Better science/technology/application/product
 - ✓ Law/IP - Better IP filing/protection/management/utilization; Better litigation/licensing/enforcement...
 - ✓ Business/Leadership/Management - Better financial management, Product development, Better marketing and sales, Creative idea, Creative strategy, execution...

US FDA is a Relatively Innovative Organization

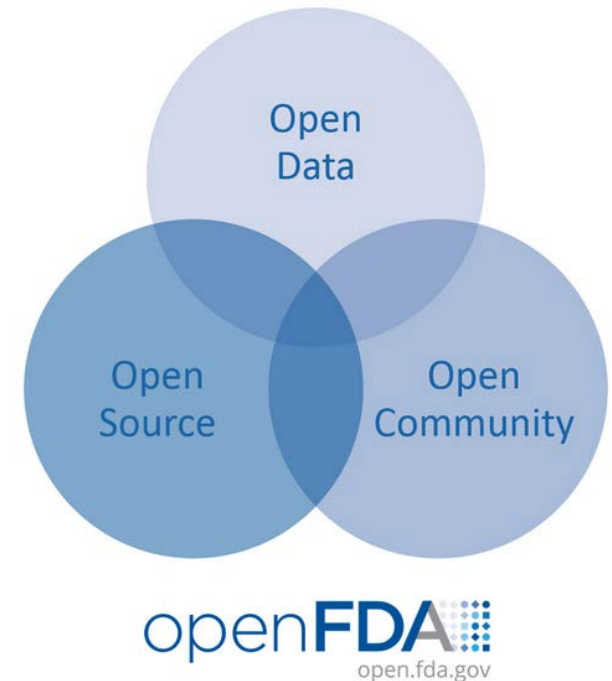
Creative Regulatory Process

- US Healthcare product approval is governed by US FDA FD&D Act and its subsequent amendments (and related laws)
- **Some examples of FDA initiatives to speed up approval:**
 - ✓ Clear and transparent communication, firm commitment, clear guidance and Freedom of Information Act (FOIA)
 - ✓ Emergency IND, Exploratory IND, Investigator IND, Accelerated/Expedited approval, Priority approval, Rolling application, Protocol assessment...
 - ✓ PDUFA I-V, GDUFA, BsUFA... [quicker and more efficient approval]
 - ✓ Critical path initiative, surrogate endpoints, biomarkers initiative...
 - ✓ Scale-Up and Post-Approval Changes (SUPACs for formulations)
 - ✓ 1986 BE hearing, Generic Initiative for Value and Efficiency (GIVE), generic protocol review,, correspondence and citizen partition review, fax-on-demand, regulatory consultation meeting to resolve industrial issues, quarterly meeting with industry, drug specific guidance, BCS classification, highly variable drugs, long half-life drugs, food studies, special dosage forms...

Most Recent Innovative Initiative Regulatory Move

OpenFDA – Open Data, Open Source, Open Community

- Use **public FDA data** in both the public and private sector to spur **innovation**, further regulatory or scientific missions, educate the public, and save lives [June 2, 2014].
- The FDA has publicly released a huge amount of data on drug side effects that it hopes will lead to new applications and research.
- The move to make medical data more transparent isn't limited to the FDA. Several drug makers working with the National Institutes of Health have begun releasing clinical trial data in a limited fashion to help find new uses for old drugs.



Creative Government and Spirit of the Law

Correct, Modify, Improve for the Sake of the Country

- In September 16, 2011, President Barack Obama approved the biggest reform to the US patent system in nearly 60 years [**Leahy-Smith AIA**]. “Here, in America, our creativity has always set us apart, and in order to continue to grow our economy, we need to encourage that spirit wherever we find it,...” the president said, minutes after putting pen to paper.



Spirit of the Law
Spirit of the Government

- On January 14, 2013, President Obama signed **AIA Technical Corrections Act** into law - to correct and improve certain provisions of the Leahy-Smith AIA. The new Act corrects several minor errors, but also includes important changes other provisions of the Patent Act
- The Public Health Service (PHS) Act of 1944, the Biologics Price Competition and Innovation (BPCI) Act (Biosimilar Act) of 2009, The Patent Protection and Affordable Care (PPAC) Act of 3/23/2010, Biosimilar User Fee Act (BsUFA) of 2012

Creative Bully 每個國家的政府絕對圖利國家本土企業及廠商, ECFA, TIFA, TPP...

- TPP: Trans-Pacific Partnership
- 每個國家捍衛本國利益、扶植本土企業不遺餘力
- 美國國務卿 Hilary Clinton 公職期間出國數百次、每次帶領不下百名美國企業家，圖利本土企業，為美國經濟打拼
- 政府圖利本土企業廠商 - 天公地義；我們要防止的是圖利某一特定廠商
- 苛政猛於虎、扯後腿的政策、只會防弊而不興利的政府更猛於虎

08/14/14

美捍衛專利藥年限 卡住TPP

錙銖必較 高品質低效率

【新加坡記者林以君／十日電】製藥業帶來的龐大商機，美國對藥品專利保護年限的堅持，可能變成「跨太平洋夥伴協議」(TPP)今年十月難以完成談判原因之一。來自美國等十一國的談判代表，本月四日起在新加坡舉行TPP第十六回合閉門談判。馬來西亞貿易部長穆斯塔帕·穆罕默德(Mustapa Mohamed)在新加坡外賓記者協會說，「達成目標變得困難、更有挑戰性，這也可能無法在二〇一三年十月準時完成談判。」三月六日在一項與該項談判有關的「利害關係人」議題發表會中，製藥業者幾乎占了四分之一，投入

龐大財力研發新藥的藥廠，與代表發展中國家人民的「非政府組織」，彼此對TPP是否引用美國現行十二年專利保護期限立場鮮明。大藥廠投資研發藥品並取得專利，希望在專利期限內獲利；與專利藥相對的「生技仿製藥」或「學名藥」，是在原廠藥專利過期後，其餘藥廠以同樣成分、製程，生產藥效相同的藥品。人道組織「無國界醫生」要求發展中國家談判代表，拒絕美國推動的專利規定，讓學名藥生產能更早上市以造福更多人。「無國界醫生」組織引用一份外洩的草案，內容指美國談判的立場

就是「壟斷保護，以維持高藥品價格」。該組織也說，美國談判代表在TPP一度主張對現有藥品修改專利期限達廿年，將更難取得便宜的藥品。兩方對專利期限的看法差距，影響病人是否能以更便宜的價格取得藥品。以二〇一〇年為例，目前的十個TPP會員國間就有三千五百五十億美元的藥品產業價值，美國公司又占其中八成。「美國藥品研究與製造協會」(PhRMA)表示，研發新藥需要十到十三年以及十億美元經費，也不是每項研發都能成功，錢砸下去，常什麼結果都沒有。

新加坡記者林以君
生技產業是美國在經濟衰退時，少數能夠持續增加雇用員工人數的產業之一。若是美國談判代表無法為麻州超過五百家生技及製藥產業提供合理的全球性智慧財產權保護，奢談強化全球競爭力。
生技製藥業外，農產品開放、汽車工業的談判，也有類似掙扎。日本安倍內閣可望在十三日宣布加入TPP談判，最快也是年中才會加入談判，但光是日本稻米市場與日系汽車工業開放，對美國的衝擊就非常天。

日本加入TPP談判，也引起另一個前兩年倡議國擔心的問題。去年四月，紐西蘭的TPP談判代表摩爾(Mike Moore)就擔心，其他主要經濟體若是中途加入TPP談判，可能拖緩談判速度。
新加坡當時的談判代表陳慶珠也建議，若不設定期限，TPP談判會沒完沒了。澳洲當時代表畢斯利(Kim Beazley)也同意，因為世界貿易組織(WTO)多哈回合談判無限期延期，股鑑不遠。
畢斯利當時指出，先談好內容再讓想加入的國家加入，才是王道。

TPP被稱為「高品質」自由貿易協定。但高品質內容與高效率進度，不一定成正比。
TPP協定談判同時涵蓋傳統貿易及新興貿易議題，傳統議題如關稅逐年降低已是基本入會條件；類似製藥業面對專利期限，還有勞工、環保這類非傳統議題，都牽動各國內法規調整。
國際貿易談判依各國經濟利益，即使是開發程度較佳的國家，依然錙銖必較，壁壘分明；TPP想在短時間內畢其功於一役，絕非易事。

Keith Chan, Ph.D.

11

Innovation and Product Development

What Make Them a Worldwide Success?

In January, originally planned to give two shows in Hong Kong but the 12-Girl Orchestra held four instead to accommodate the number of fans.



20 CHINA PICTORIAL



Think outside the box,
be different, nothing is
impossible

Creative Science, Creative Products, Creative Business (Pharmaceutical is no Different)

- Slow-K[®] (KCl, Ciba-Geigy, now Novartis)
- Transderm Nitro[®] (Nitroglycerine Transdermal Patch, CG), Transderm Scop[®], Estraderm[®], Habitrol[®], etc. [Old Chemical, New Use]
- Xyponex (levalbuterol), Xyzal[®]/Xusal[™] (levocetirizine), etc.
- Clarinex[®] (desloradadine), Allegra[®] (fexofenadine), Nexium[®] (esomeperazole), etc. [Old Drug New Isomer, New Metabolite]
- Rogaine[®], Viagra[®], Thalomid[®] (Thalidomide for ENL), etc.
- New indications: Paxil[®]; Prozac[®] -> SAD, PMDD, etc.
- Wellbutrin[®] -> Zyban[®]; Prozac[®] -> Sarafem[®], etc. [Failed/Old Drugs, New Life]
- Technology superiority is good but niche creativity is better
- **Creativity is limited only by your own imagination**

Innovation and Product Development

What Make Them a Success and You Are Not?



- Now the technology can be applied to vet medicines and vaccines
- Why can they do it and we can't?
- **Opportunity is for the prepared mind**

Opportunity is Everywhere

(May be right in front of your eyes - can you see it?)

MASS APPEAL
IT'S ON THE TIP OF YOUR TONGUE
As more medicines take the form of "edible film," the market is exploding

BY ARLENE WEINTRAUB

HEY'RE LITTLE GREEN patches of film that melt instantly on your tongue, has been driven by the Thin Strip," Brian McNamara, a president at Tervis Consumer Health in Parsippany, N.J. In the past year, retail sales of T

retail sales of set \$100 million a year ed to hit at least \$350 says James Rossman, a sible film who is now a rpa. In 1999 sales were mostly from niche prod- ible underwear that's a t bachelor parties. "Las- market wide open," who, by the way, in n inventing some of dies. eer drugmakers are e into tired brands sm into flavored viss pharmaceu- tis introduced heratha Thin it followed in Strips, nearly 30- The Tri- se now are of the and cold t time since has broken the ost of the growth

LAPPING IT UP
Pets and kids are prime targets

Gas-X. "If you have a meal that you know is a precursor to a

Some meat manufacturers are us to cure and glaze ham. There troyte strips that athletes can coi lieu of sports drinks to fight tion. Film might someday b a moisture barrier, separate tomato sauce from the cr frozen pizza, for example crust stays crisp. "These l improve the quality and sh food," says Tara McHugh, leader for an Albany (Calif the Agriculture Dept.

And get this: Matthew owner of Origami F Pleasanton, Calif., has d films made of carrot, an with basil, which can b place of seaweed to wt "Some people have sion to seaweed, or want an alternative," reasons. Costco W Co. is testing sushi in de Bord's films at its stores in Ca er how the play in Tokyo. ■

4 9:43PM

4 9:48PM

Why didn't I thought of this before? Who should be blamed?

Innovation Has No Limitation

Fast-Dissolving, Slow-Release to Teeth (Overnight) Strips



FOR EASY WHITENING IN

Noticeably whitens teeth and kills bad breath germs
Same enamel-safe ingredient used by dentists
Strips dissolve in 5-10 minutes on average
with no mess and nothing to remove
Use twice daily for two weeks

Easy to Apply

For lower teeth*
position notch in top left

For upper teeth*
position notch in bottom right

Tear across to remove strip from pouch.

Align edge of strip with gumline, press and fold behind teeth.

*Whitening ingredient is only on one side of strip.
Strips are designed to work on either upper or lower teeth.

Smile and Go!

By All Means, Explore...

Now Creative Diseases...

**Frustrated by frequent urges in your internal plumbing?
Annoyed you can't always do things spur of the moment?**

There's a treatment you can discuss with your doctor.

Frequent bladder urges can sometimes get in the way of doing things spontaneously. So talk to your doctor today to see if prescription VESicare can help.

Taken once a day, VESicare can reduce frequent urges and may help effectively manage bladder leakage, day and night. It doesn't have to be a pipe dream.

**Call (800) 403-6565
vesicare.com**

Here's what you'll receive:

- Information about overactive bladder
- \$25 savings check*
- Talk to your doctor guide

Important Safety Information

VESicare is for urgency, frequency, and leakage (overactive bladder). VESicare is not for everyone. If you have certain types of stomach, urinary, or glaucoma problems do not take VESicare. While taking VESicare, if you experience a serious allergic reaction, severe abdominal pain, or become constipated for three or more days, tell your doctor right away. In studies, common side effects were dry mouth, constipation, blurred vision, and indigestion.

Please see important product information on the following page.
*Subject to eligibility. Restrictions may apply.

VESicare
(solifenacin succinate)
tablets

If you don't have prescription coverage, visit pprx.org, or call 1-888-4PPA-NOW (1-888-477-2669)



Overactive Bladder - GSK

FLOMAX
WEB SITE

Patient Information | Full Prescribing Information

There are millions of men over 50 with the symptoms of BPH.²

Print This Page

Welcome to 4FLOMAX.com - where you can find important and relevant information about male urinary symptoms due to BPH (Benign Prostatic Hyperplasia). If you're experiencing symptoms such as going often, going urgently, weak stream and frequently waking up at night to go, you could have BPH (also known as enlarged prostate). This Web site will help you learn how BPH is diagnosed, how FLOMAX may improve the symptoms of BPH in one week, how to talk to loved ones about BPH, and much more.

Matter of FACT
BASICS

Sign up now and get up to **\$15** in savings. It's free and easy!

Male urinary symptoms due to BPH affect different people in different ways - including people who care about men with symptoms. How BPH affects you and your loved ones has everything to do with who you are and how you want to live your life. Please click the button below that best describes your situation.

Click here to see our TV commercial.

I may have male urinary symptoms.

I care about someone who may have male urinary symptoms.

I am currently taking FLOMAX for my male urinary symptoms.



Important Safety Information

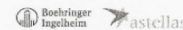
FLOMAX is approved to treat male urinary symptoms due to BPH. Only your doctor can tell if your symptoms are due to BPH and not another condition such as prostate cancer. Common side effects of FLOMAX are runny nose, dizziness and decrease in semen. A sudden decrease in blood pressure may occur upon standing, rarely resulting in fainting. So when starting FLOMAX, avoid situations where injury could result.

Before taking FLOMAX capsules, please see the [Patient Information](#) and full [Prescribing Information](#).

¹ FLOMAX Prescribing Information, Boehringer Ingelheim Pharmaceuticals, Inc. 10/05.

² Decision Resources Patient Base, March 2005.

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Content intended for U.S. residents only.
FL11548

Male Urinary Symptoms – BI caused by BPH (Benign Prostatic Hyperplasia)
Also Uroxatral - Sanofi-Aventis, Avodart - GSK

Creative Disease

Restless Legs Syndrome (RLS) – anti parkinsonism drug



- **Requip® (ropinirole HCl) 0.25, 0.5, 1, 2, 3, 4, 5 mg tablets by GSK is the first FDA-approved medication for the treatment of moderate-to-severe primary Restless Legs Syndrome, or RLS (15 or more episodes monthly)**

Creative Science, Creative Products, Creative Business, and Now Creative Diseases



- Obsessive compulsive disorder (OCS) - Prozac
- Premenstrual dysphonic disorder (PMDD) – Sarafan, Paxil
- Social anxiety disorder (SAD) – Paxil, Zoloft, Prozac
- Children and adults attention-deficit/hyperactivity disorder (CHADD) – Ritalin, Adderall, Strattera
- Male erectile dysfunction (Male ED) – Viagra, etc.
- Male pattern baldness (MPB) - Rogaine
- Female sexual dysfunction (FSD) – Viagra, Testosterone
- High cholesterol – Mevacor, Zocor, Lipitol, etc.
- Inadequate or not enough eye lashers - Latisse
- Others (Overactive Bladder; Restless Legs Syndrome, etc.)

Common Techniques of LCM

The Role of Government, Industry and Scientist

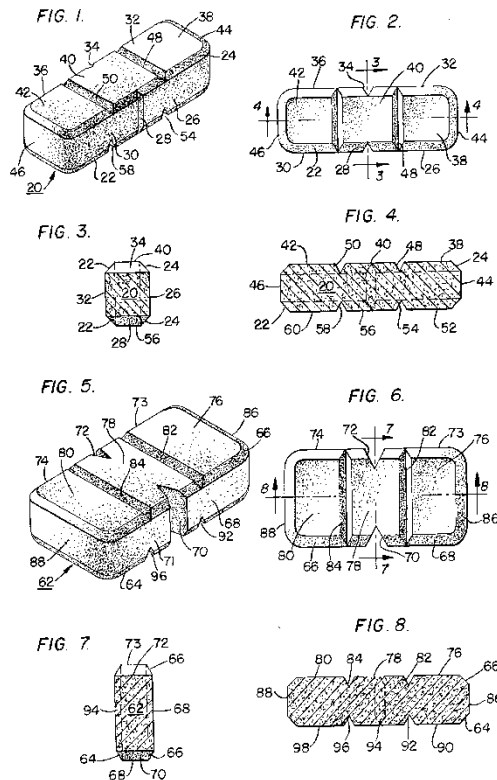


- Better science, line extension, family of products, expertise
- Brand building, pricing strategy, aggressive M&S
- Patent, market and data exclusivity management
- FDA management
- Litigation as entry barrier, no forever friend, no forever enemy, do everything anything to keep the money
- Authorized generic, blurred the line between brand/generic
- Federal and State legislators (politicians management)
- HMO re-imburement, insurance pricing and purchasing strategy
- USP management
- Others - innovation has no limitation

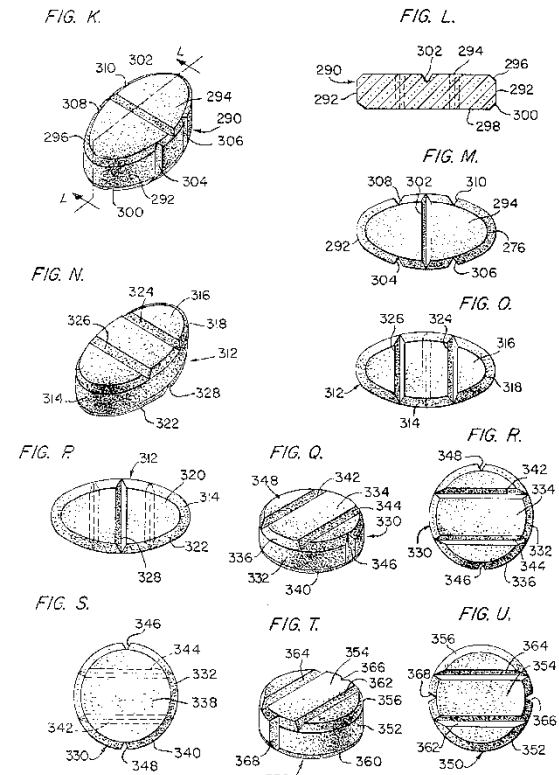
Innovation in Patenting...

Targeted Innovation 每個IP的建立與應用都可以靈活運用，存乎一心

U.S. Patent Jul. 29, 1980 Sheet 1 of 2 4,215,104



U.S. Patent Mar. 24, 1981 Sheet 2 of 3 4,258,027



How many ways to split a tablet into three equal parts?

Summary - Innovation is Simple

創新其實很簡單... (Thinker + Leader + Doer + Rainmaker + Execution)

- **Innovation has no limitation** 創新並無界限，工作領域，年齡，性別，種族的限制
- **Innovation is not just talk** 創新並不是一個口號，是要你身心力行，每一分每一秒都要想如何與人不同，如何改善已有的或是沒有的東西 (Innovation - 不要做乖寶寶, 試試逆向思想)
- **Innovation is to walk your talk** 然後付之實踐 (Product Development – Leader and Management Team)。你可能有很多失敗，但總有一天，總有一次會成功，你就是一個成功的創新者
- **Protection and commercialization** 保護與商業化
- **Innovation is actually very simple** 創新其實很簡單...