



**Alcon®**

Research & Development



March 3, 2006

**Jerry Cagle  
Scott Krueger  
Robert Stevens**

# R&D Areas of Experience

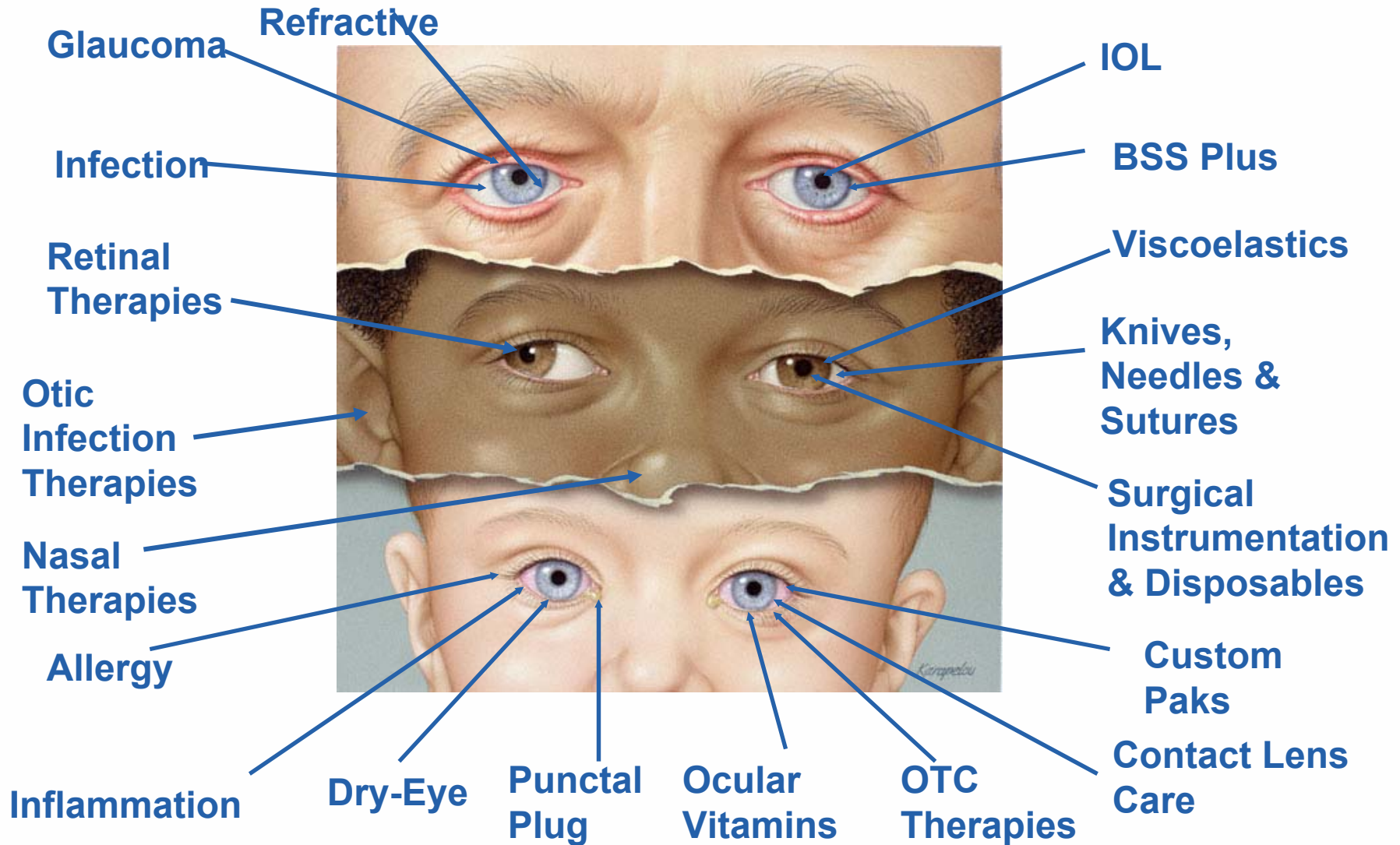


**PHARMACEUTICAL  
THERAPIES**

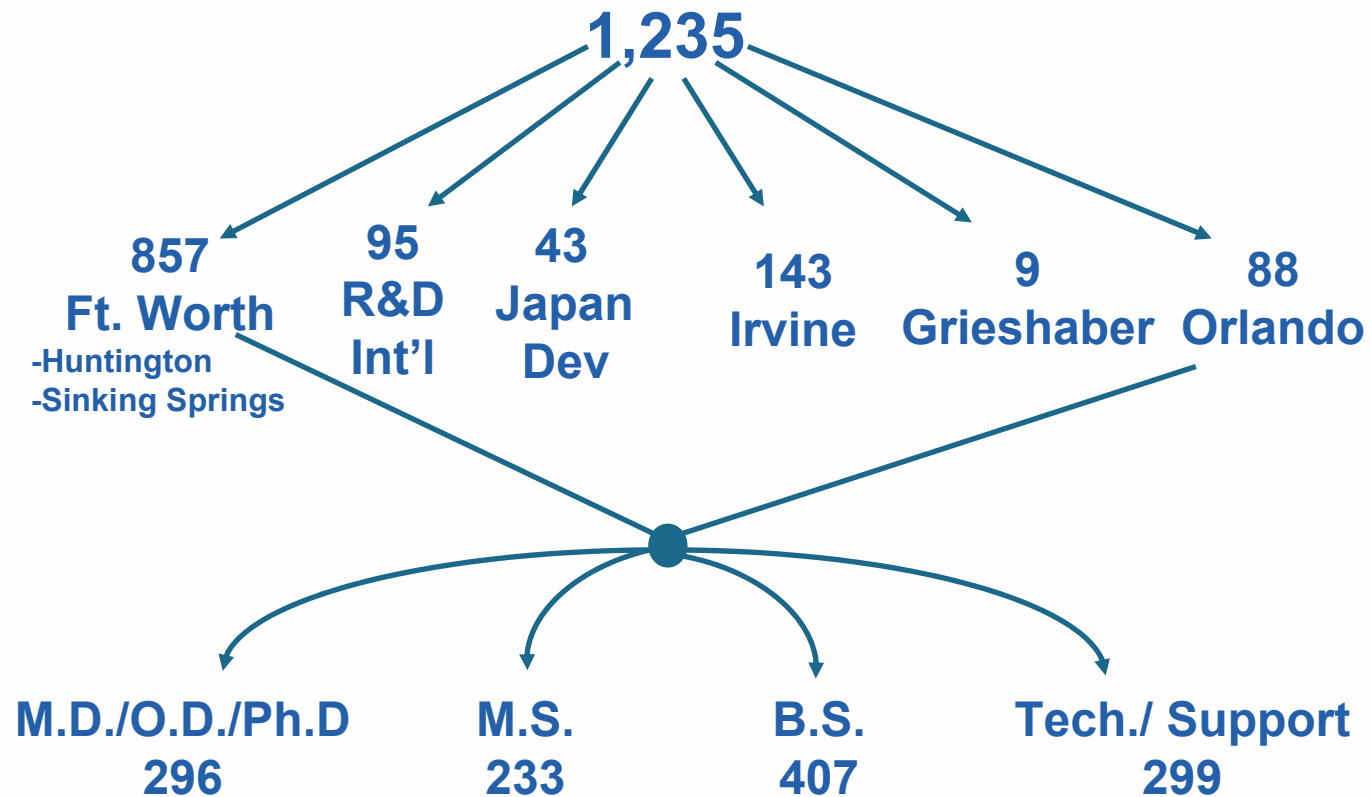
**SURGICAL  
THERAPIES  
AND  
DEVICES**

**CONSUMER  
PRODUCTS**

# Alcon R&D Focus



# R & D Organization





# Worldwide Ophthalmic R&D Sites



Fort Worth



Orlando



Irvine



Barcelona

**~1,200 Employees**

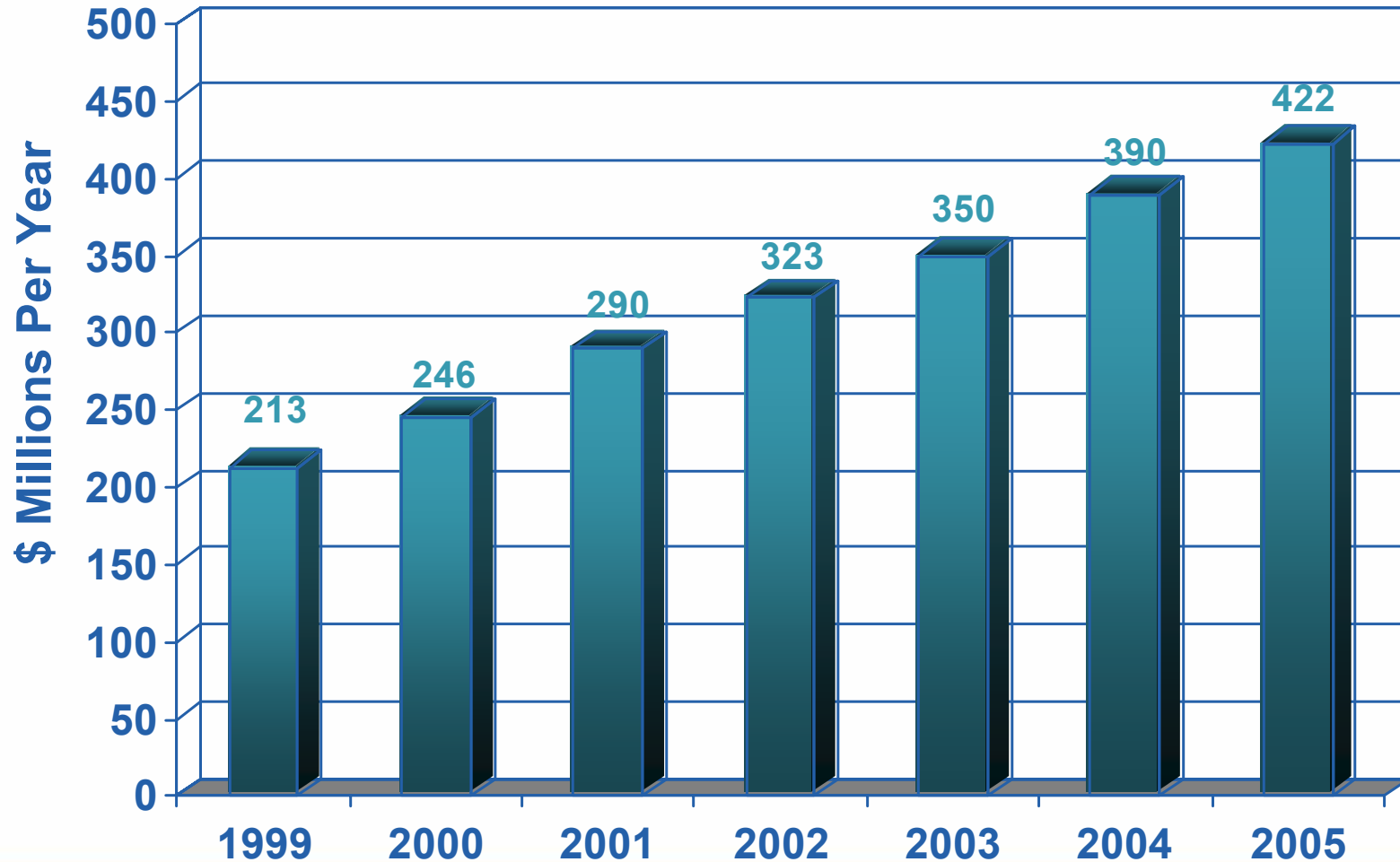
**Facilities in Texas, California, Florida, Spain**

**~ 250 Product Registrations/year**

**Next 5 years = \$2.5 Billion in R&D**

# Commitment to R&D

## 1999-2005





**Alcon**<sup>®</sup>  
Scott Krueger



# Agenda



- Glaucoma
- Dry Eye
- Retaane
- Patanase
- Anti-infective/Anti-Inflammatory



# Product Pipeline



## Glaucoma

Travatan Dosing Aid (US/EU)



DuoTrav (EU)



Travatan BAC Free (US)



Travatan (Japan)



## Dry Eye

15(S) Hete



TBD

Rimexolone

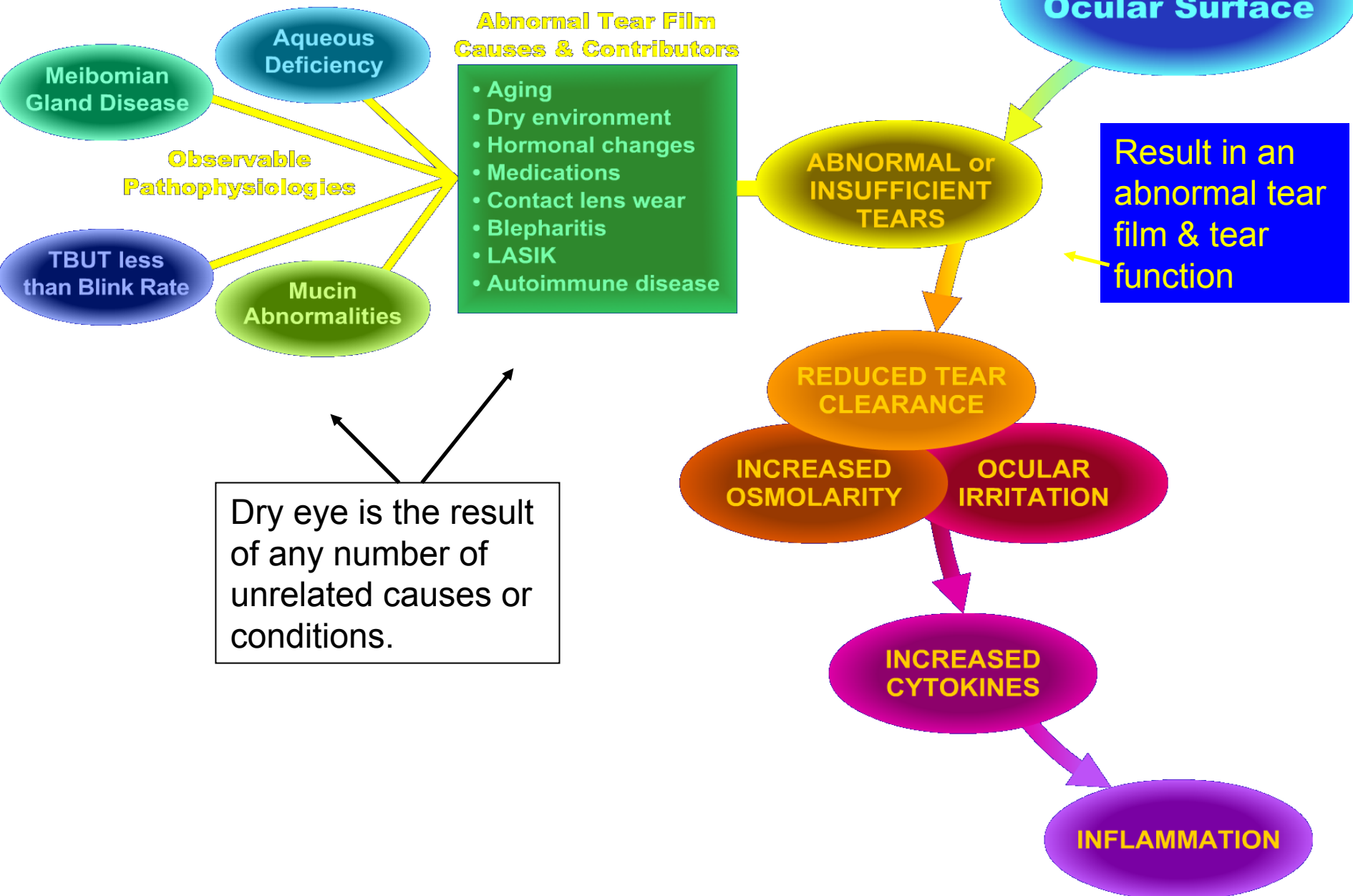


2006

2007

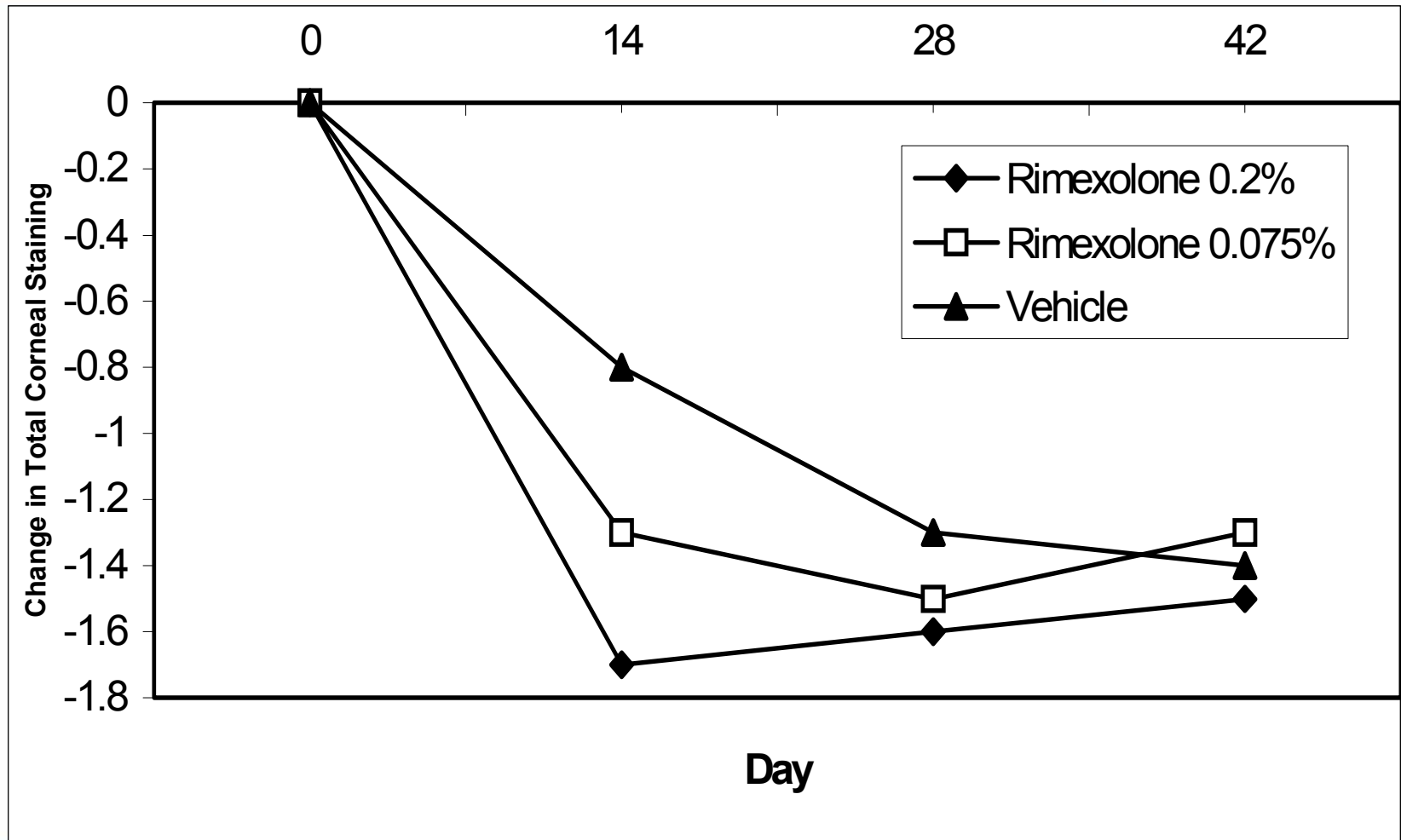
2008+

# Dry Eye Disorder

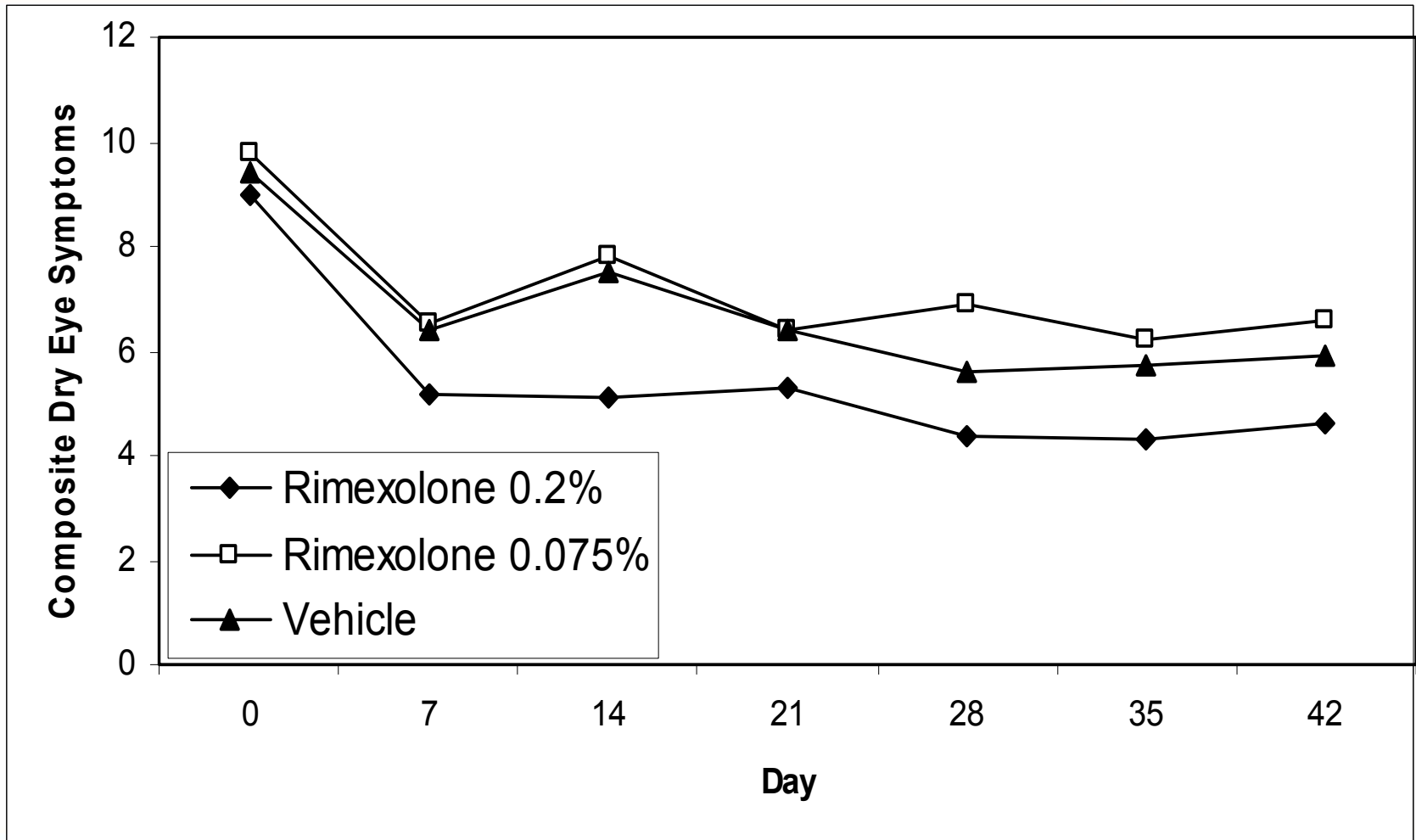


# Rimexolone

## Change in Total Corneal Staining



# Rimexolone Composite Dry Eye Symptoms



# Retaane Update



- Retaane approved in Australia 12/05
- US and EU request additional data from ongoing or new studies
- Studies in progress and planned
  - IDEAA dose regimen study
  - NEI study with monoclonal antibody VEGF inhibitor
  - EU placebo controlled study
- AART - Risk Reduction Study
  - Fully enrolled Jan 2006
  - 2596 patients
  - 4 year study



# Patanase Update



- FDA requested reformulation of Patanase
  - Formulation issue unrelated to Patanol
- Met with FDA to discuss pathway forward
  - Very satisfied with efficacy
  - Ensure safety in expected broad use
- Next Steps
  - Reduce Inactive Ingredient
  - Clinical Studies
  - Amend NDA 2007

# Product Pipeline



## Anti-Infective/Anti-Inflammatory

Vigamox (Japan)



Moxifloxacin AF (US)



Moxidex Otic (US)



Moxidex Ophthalmic (US)



2006

2007

2008+



**Alcon®**

Jerry Cagle



# Alcon is Positioned for Long Term Success



- Diseases of the aging eye represent one of the last great areas of unmet medical need
- Favorable demographics
- Significant resources for drug discovery research
- Broad internal expertise in all areas
- Extensive relationships with institutional researchers

## Glaucoma

- 1-4% of population over 40
- 67M patients worldwide, 5-6M in US
- 7M are bilaterally blind from glaucoma

## Dry Eye

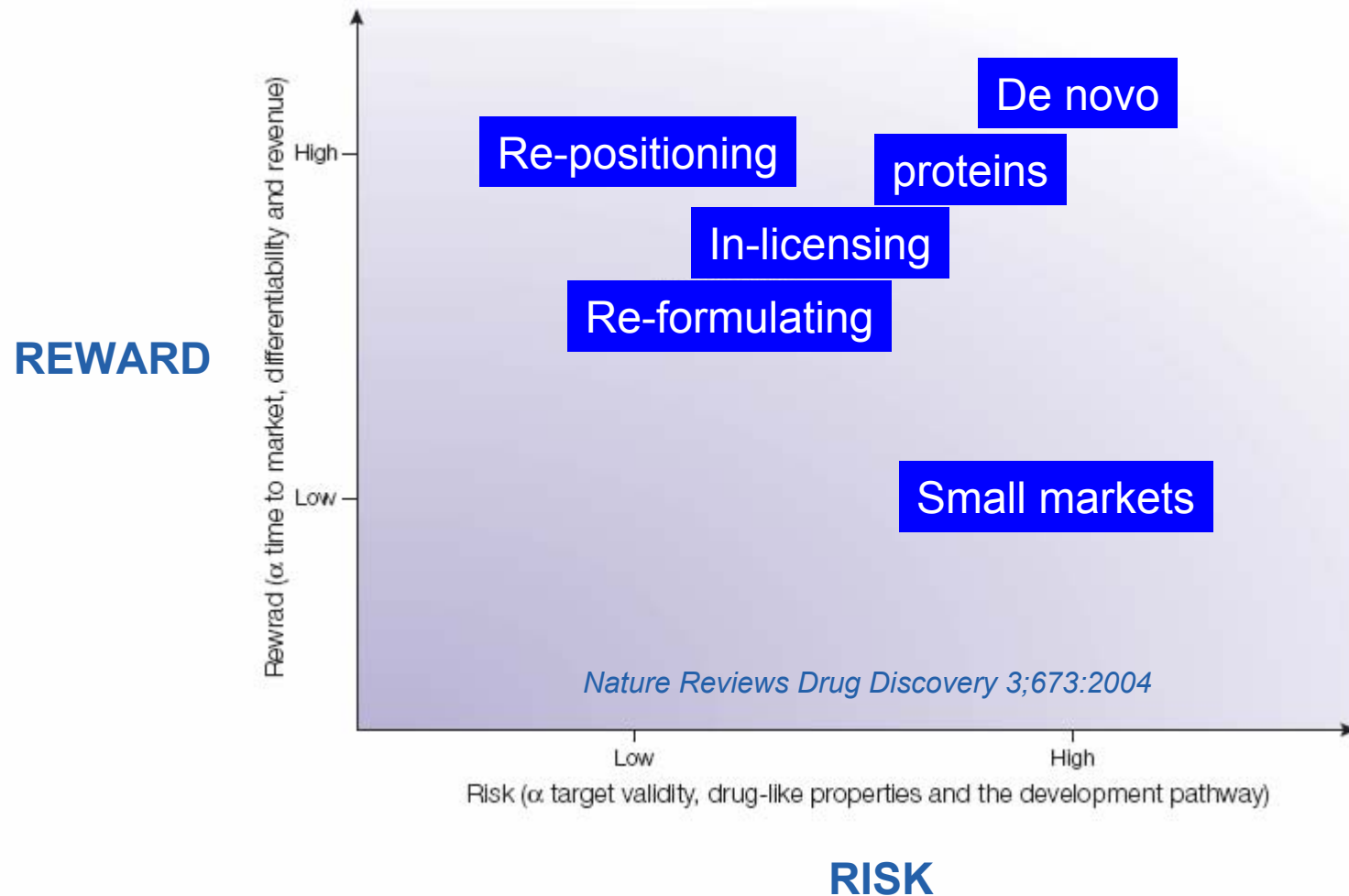
- Estimated 40-60M in US with dry eye
- 16M diagnosed; 39M undiagnosed
- Approx 7M are moderate to severe

## Retinal Disease

- 39M patients in US, EU, Japan
- 26M with AMD: 22M Dry and 3M Wet
- 13M with Diabetic Retinopathy

# A Strategic Advantage

## Mine all sources of pipeline compounds





# Focused collaborations are increasingly important

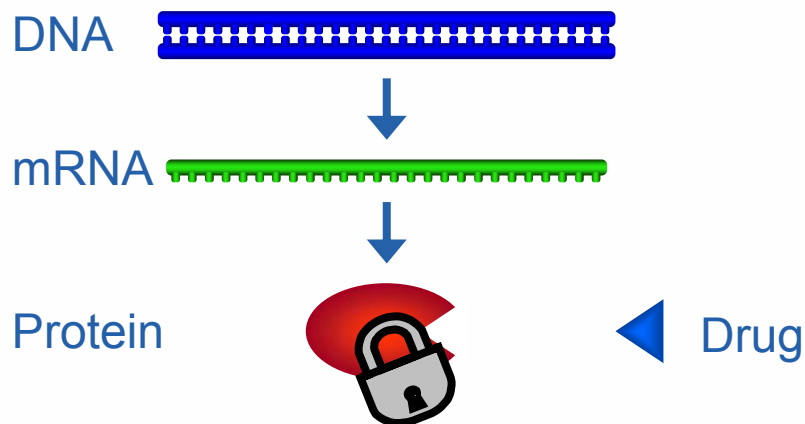


- Allow us to partner with companies whose expertise complement ours
- Technology changes rapidly. Collaborations allow us to get what we need, when we need it, with little amortization.
- “Renting” versus “Buying” allows for greater flexibility in utilizing our resources

	Glaucoma	Retina	Allergy/Dry Eye
Dharmacon (CO)	●	●	●
Albany Molecular (WA)	●		
Origenis AG			●
Jerini AG	●		
Kalypsys (CA)	●	●	●

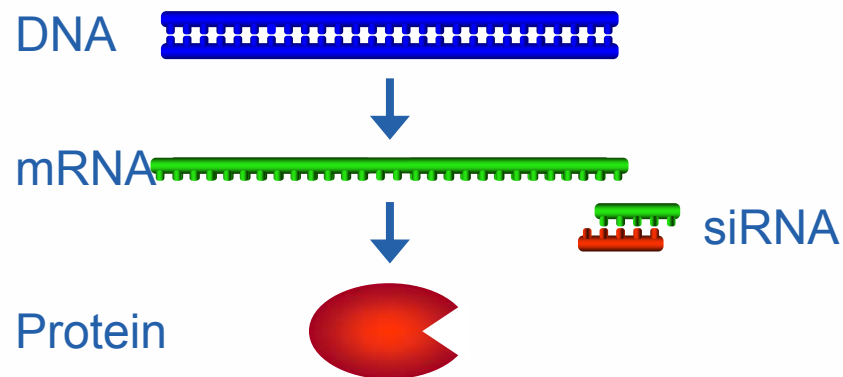
# Small Molecule Drugs vs. siRNA

## Small Molecule Drugs



- Binds to active site on protein
- Inhibit protein function directly
- 1 molecule of drug binds 1 receptor
- Relatively short duration (hours)
- May inhibit other proteins (side effects)
- Most protein structures are unknown
- Limited to “druggable” targets
- Chemical libraries are vast ( $10^6$ )

## siRNA



- Direct cleavage of mRNA
- Inhibit production of protein
- 1 siRNA can inhibit 1000 receptors
- Relatively long duration (weeks)
- Target specific
- Sequence of most human genes known
- All mRNAs are targetable
- ~1000 siRNAs/target;  $< 5\%$   $IC_{50} < 1$  nM

# Albany Molecular



**We are searching for molecules that affect water movement into and out of cells.**

Albany has expertise in natural products with the world's largest collection of natural product lead-finding libraries

A team of natural product experts with decades of experience in the field and working together

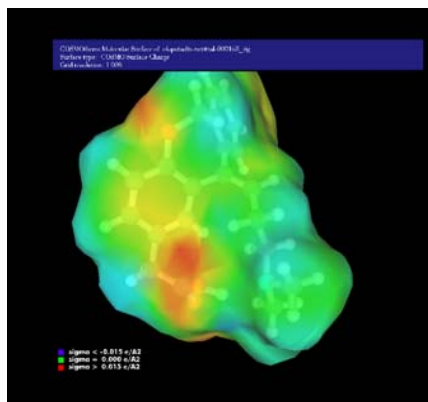
The ability to rapidly advance a natural product from hit to lead to qualified drug candidate

# Origenis: Novel Chemistry Technology



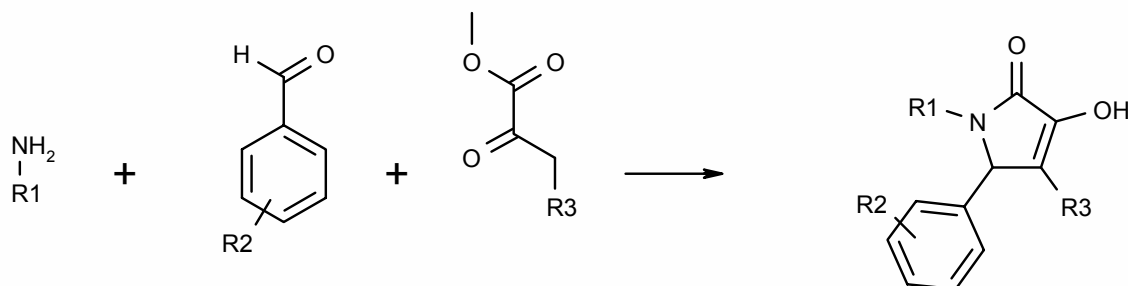
- **Conventional**

- **Structure Based Design**
- **Structures chosen based on what looks similar to parent**
- **Multiple Step Synthesis**



- **Origenis**

- **Electronic and Steric Field Based Design**
- **Structures chosen based on proprietary algorithm to select functionally similar “chemical genomics”**
- **Use of HT chemistry**



**One vessel synthesis**

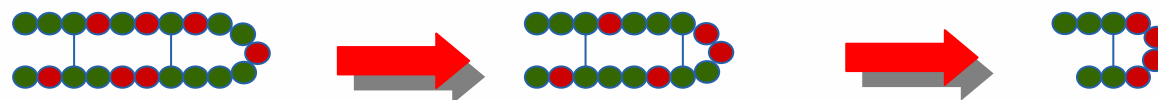
**Purification using mass triggered HPLC**

# Jerini- ANP/CNP

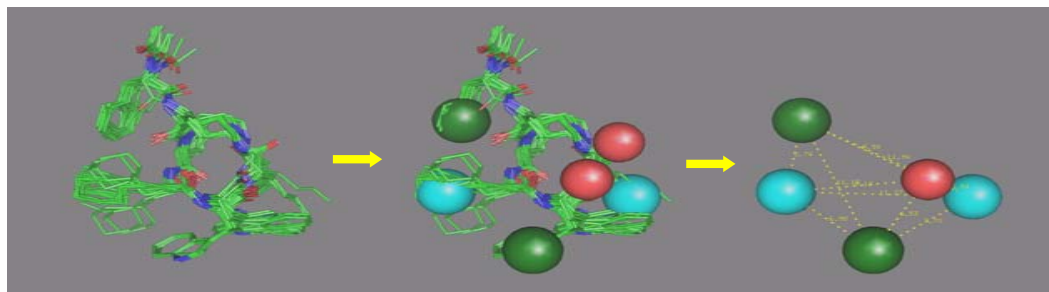
## *Jerini's P2D Process*



### 1. Minimization of peptide



### 2. Generation of non-peptide drug



### 3. Proven successes

*Bradykinin receptor antagonists*  
*Complement C5R*  
(BOTH are in clinical studies)



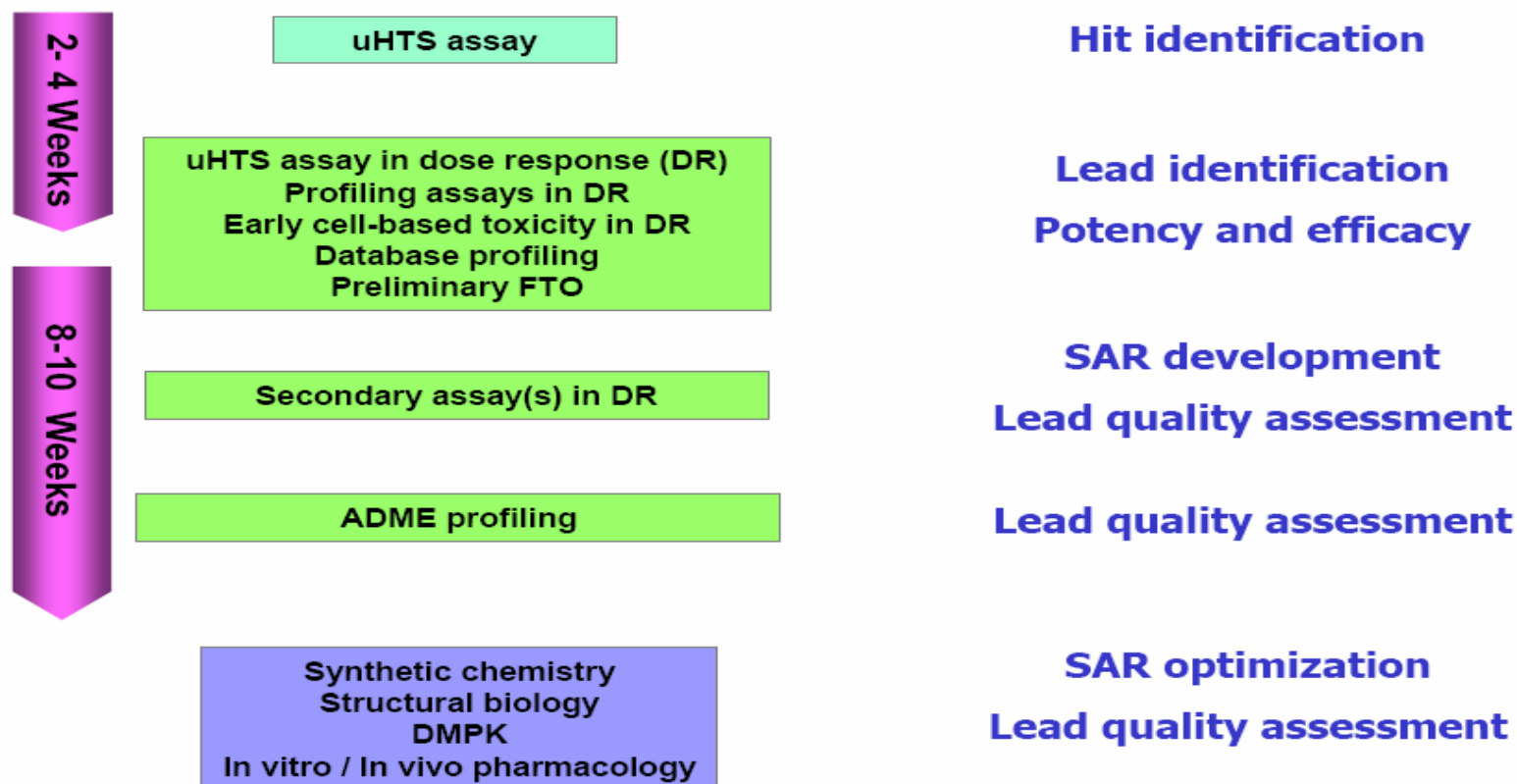
# Kalypsys:

## A powerful de novo discovery engine

**De Novo discovery requires increasingly expensive and rapidly changing technology, proprietary libraries for screening, and generous medicinal chemistry resources**

# Kalypsys: A powerful de novo discovery engine

## The Kalypsys Early Lead Discovery Paradigm



# Summary



- **The Alcon Ophthalmology Discovery Pipeline is robust and strong**
- **We are not content. We continue to seek new pharmacophore opportunities worldwide regardless of the source**



**Alcon®**

Robert Stevens



# Surgical Products R&D

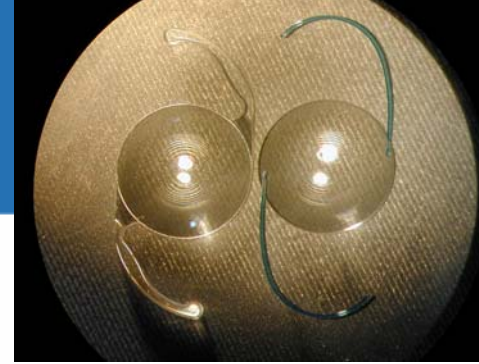
## Acrysof Franchise



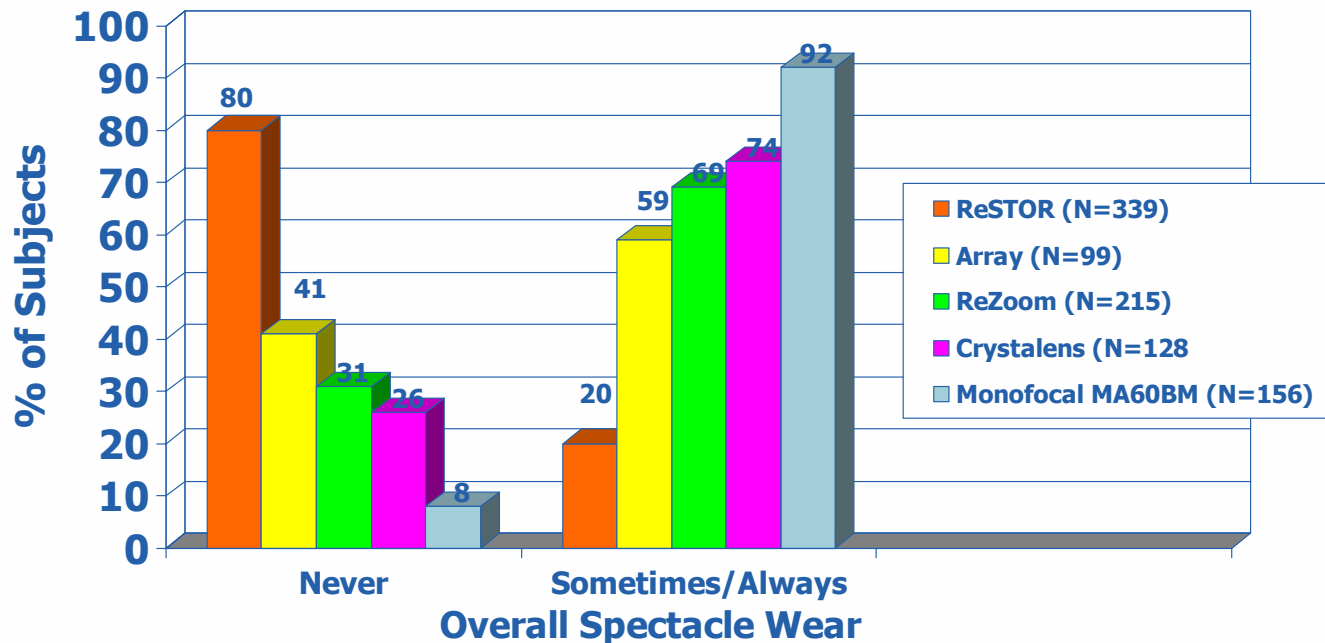
- AcrySof<sup>®</sup> ReSTOR IOL
  - AcrySof ReSTOR Natural IQ
  - AcrySof ReSTOR Natural IQ Toric
- AcrySof<sup>®</sup> Toric
- Phakic Refractive IOL
- AcrySert<sup>®</sup> Delivery System



# ReSTOR Apodized Diffractive IOL



- Novel, patented optical design
- Optic with **apodized diffractive** central zone - unique optical design matches performance to vision needs



Physician  
experience  
greater than  
90% spectacle  
independence  
with bilateral  
implantation

Patient satisfaction after  
2<sup>nd</sup> eye - 97%

Comparative S&E data

# Acrysof Toric

## Corneal Astigmatism



Corneal curvature is different in two meridians causing a defocused image

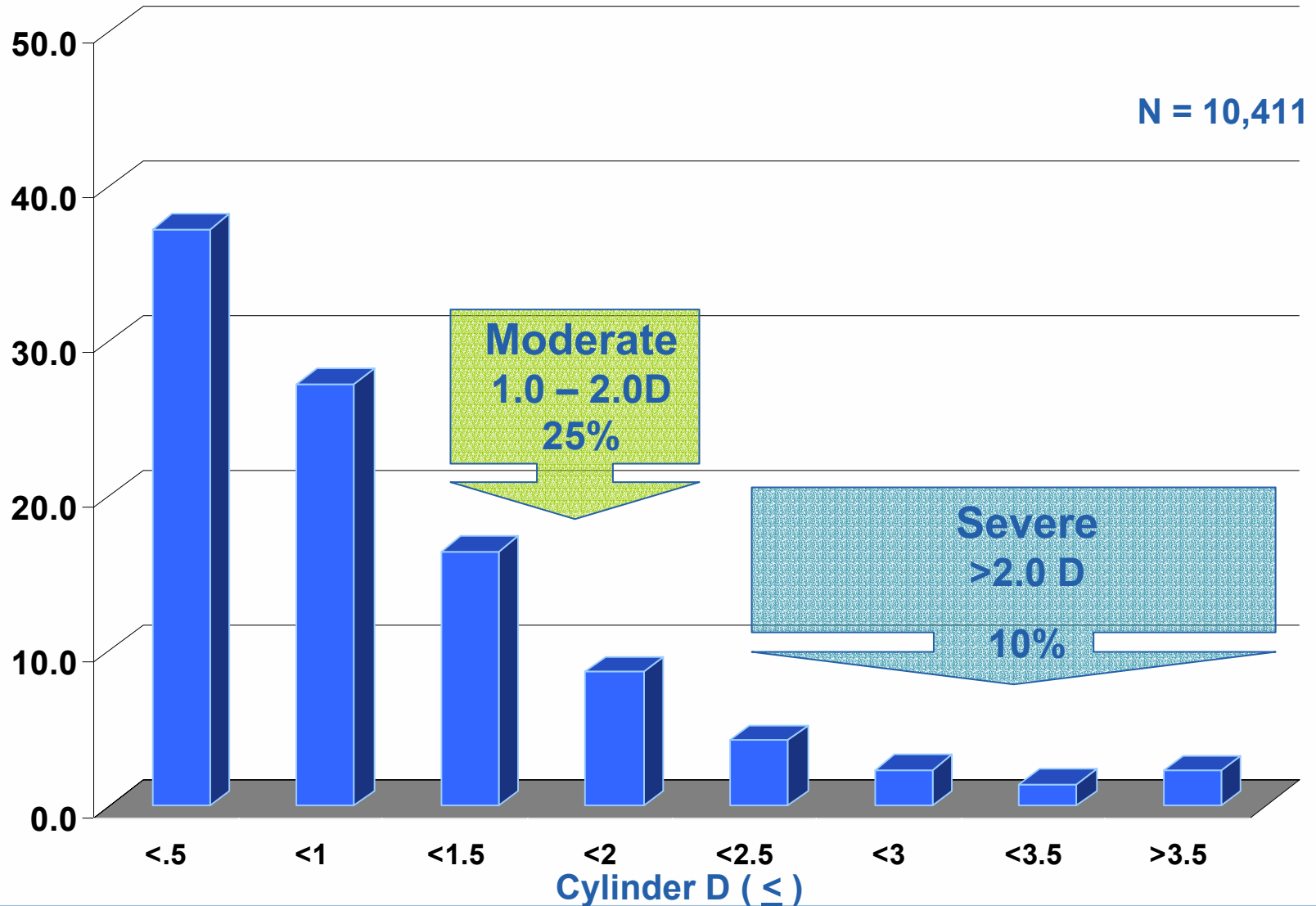
No Astigmatism



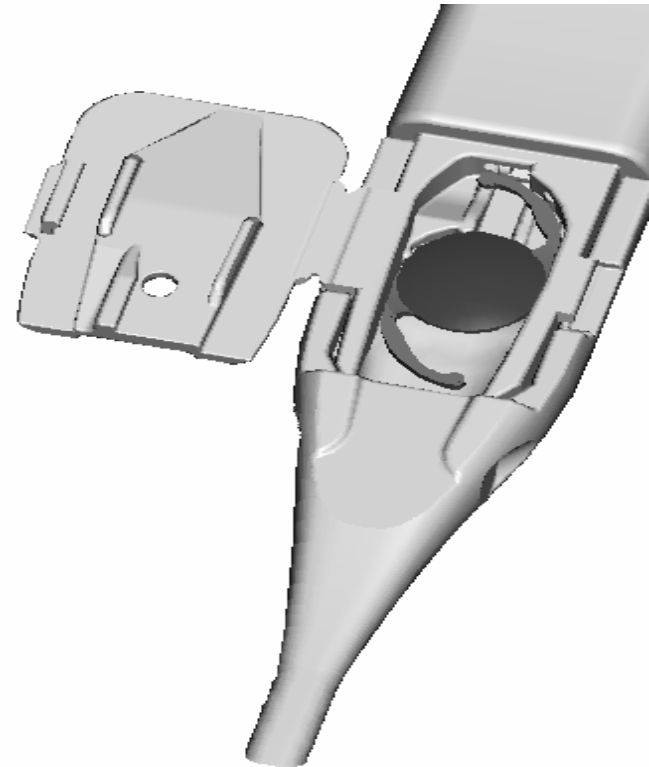
1.50 D cylinder @ 90 degrees



# Cylinder Distribution



# AcrySert® Delivery System Update

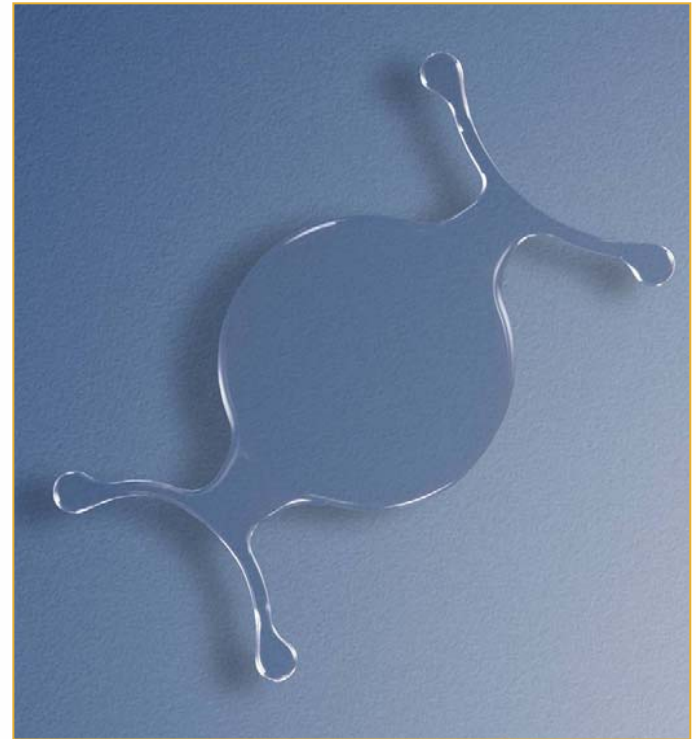


# Product Specifications

## 6.0 mm Model



Model	OAL
L12500	12.5 mm
L13000/ RA6M13	13.0 mm
L13500/ RA6M35	13.5 mm
L14000/ RA6M14	14.0 mm



**Dioptric Range: -6.0 D to -16.5 D**

# NGVS: Next Generation Vit System

- Power IV Pole
- Footswitch
- Venturi Fluidics
- Pneumatics Drivers
- Vit Cutters
- VFC Functionality
- Pak Strategy



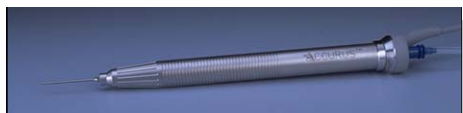
•Quick + Pack



- Monolith look
- U/S Performance
- Diathermy
- Phaco handpieces
- AquaLase
- User Interface elements
- Footswitch
- Remote Control
- Peristaltic Design Concept



- Existing Infiniti handpieces,
- Accurus Cutters and accessories
- AGS Hand Instruments



**NGVS  
Designs**

- IOP Control
- Flow control
- RFID/Barcode Reader
- eConnectivity
- Heads Down Display
- Surgical Recording (DVD)
- Integrated Audio/Video
- Volumetric Injection
- Auto Stopcock



•Laser engine

•High Brightness  
Illumination "brick"



- 25 ga vit system
- High flow infusion cannula
- AGS 25 ga DSP & 'G3'



# LADAR6000

**Development Strategy:**  
Improve ease of use and overall reliability



## Key Feature Enhancements

Improved Illumination

New Laser Engine

Improve Internal Software Linkages

High Speed Ablation

Assisted Registration

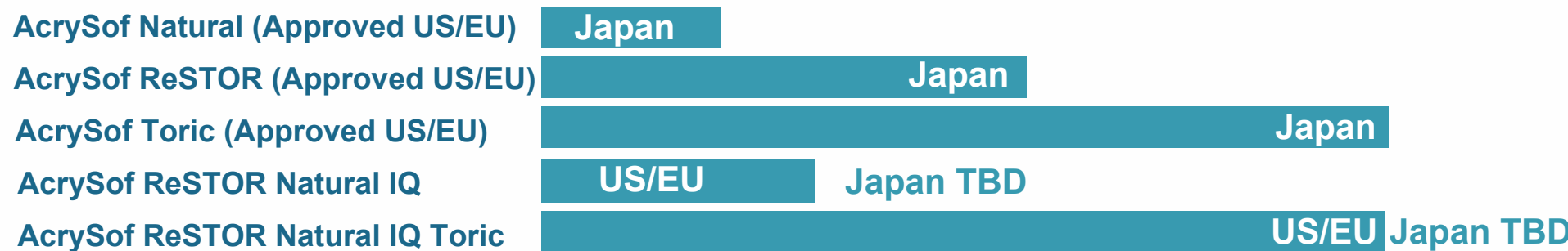
Undilated Eye Tracking



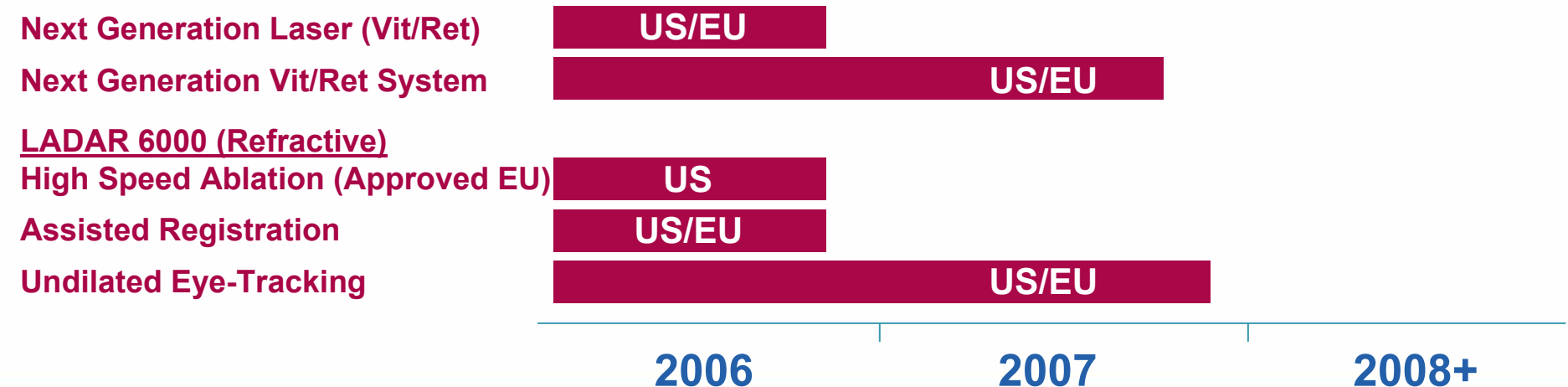
# Product Pipeline



## IOLs



## Instrumentation





# Introducing Systane Free



- No traditional Preservative
- But, Preserved in the Bottle
- And Preservative Free in the Eye
- Suitable for use day and night—  
Less blur than traditional Gels
- Comfort based on proven  
technology of recognized  
demulcents and HP-guar



# OPTI-FREE® Replenish™



- Compatible Disinfection
  - POLYQUAD® & ALDOX®
- Cleaning
  - Citrate
- Reconditioning
  - TEARGLYDE™





**Alcon®**

