

Nanomedicine: Will eyedrops be a thing of the past?

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I am co-inventor to the drug delivery system, Lipolat,
co founder of Peregrine Ophthalmic Pte Ltd

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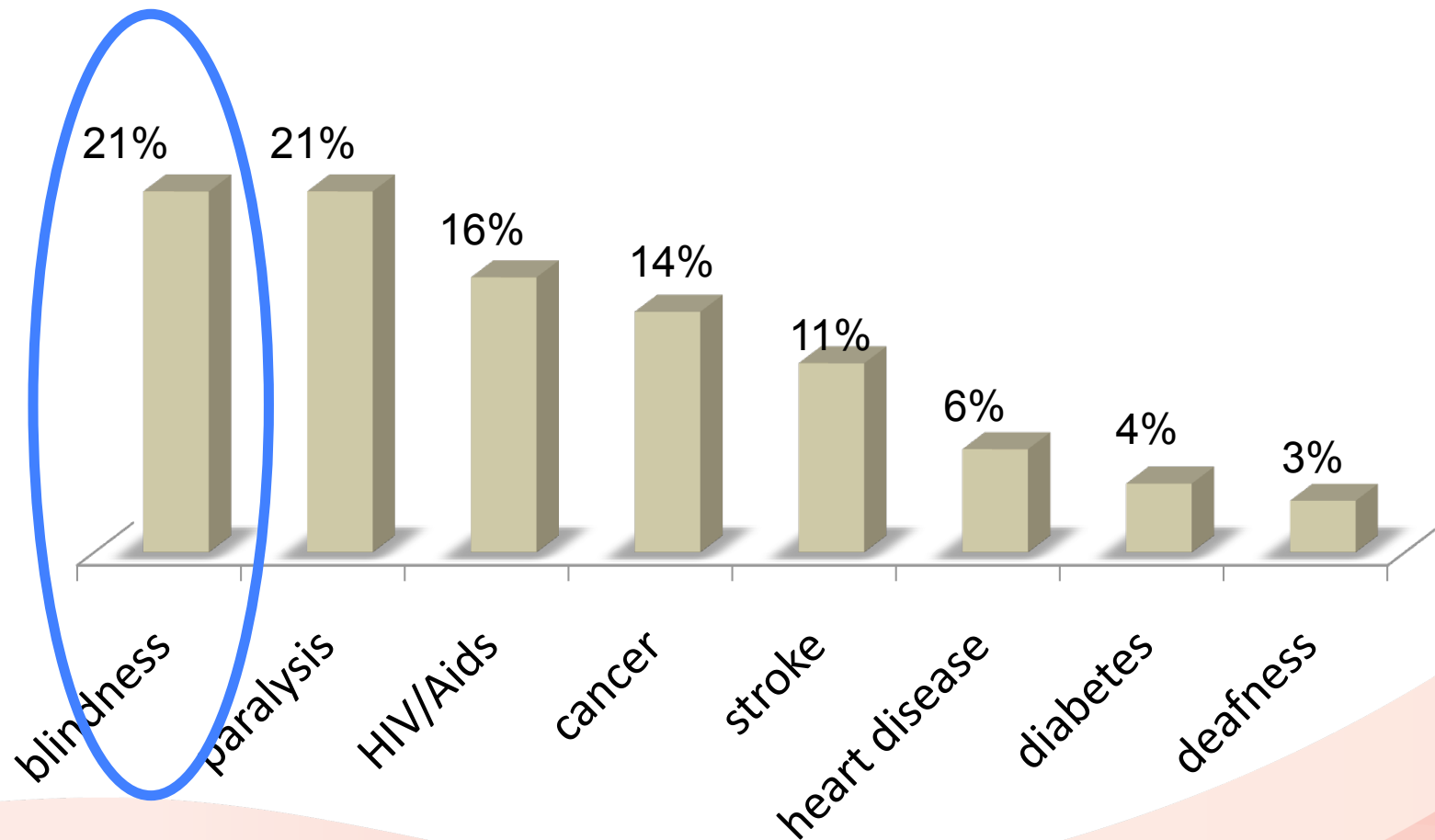
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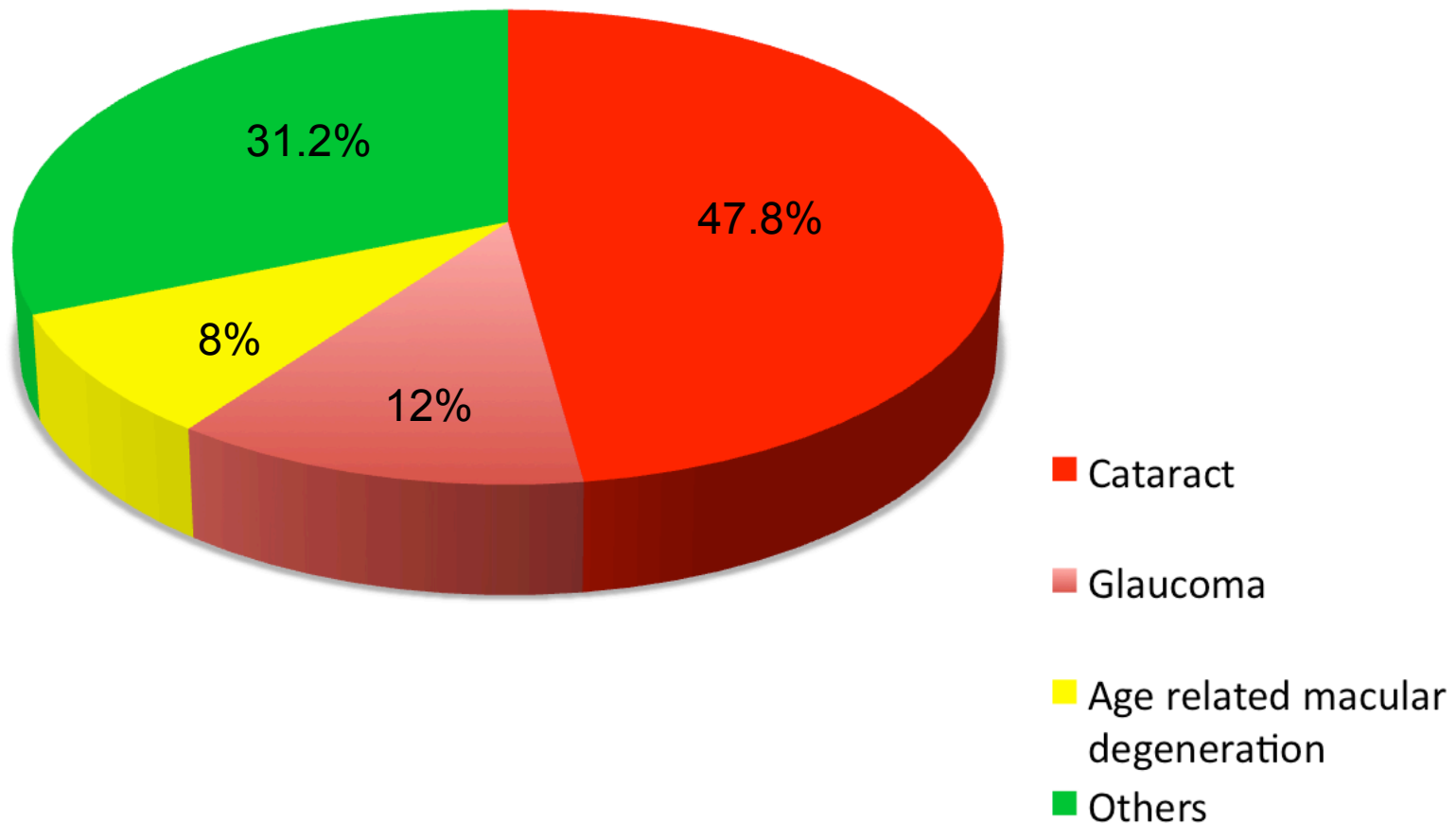
Eye Diseases

Attitudes about blindness and severe vision loss

Americans believe that loss of sight has a significant negative impact on quality of life



Major causes of blindness



Markets & Markets, 2014

SINGAPORE EYE RESEARCH INSTITUTE

Socioeconomic burden of blindness

- Loss of ability to work (significant impact in developing countries)
- Loss in quality of life
- Depression

What is Glaucoma?

Disease of the optic nerve

Vision is lost through progressive optic nerve damage from elevated intraocular pressure

Silent thief of sight

How Common is Glaucoma?

Prevalence increases with age

Age and sex prevalence:

- 1.1% Caucasians (USA)
- 2.4 %Mongolians
- 3.1 %Japanese
- 3.2 %Singaporean Chinese
- 4.7 %Afro-Carribean (USA)

How does IOP cause glaucoma?

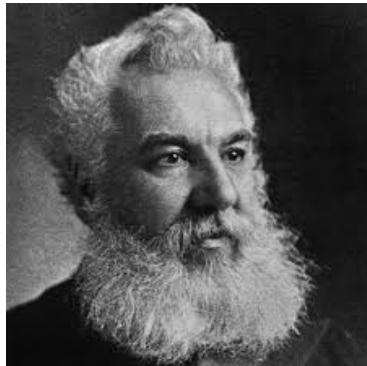
- It's all about the **FLOW**
- What goes in, must come out.....
- If not IOP builds up in the eye, damaging the optic nerve and glaucoma develops



First line treatment is eyedrops



1876



1972
to
2014



The problem with eyedrops...

Bioavailability

Side effects

Patient adherence/compliance

Poor bioavailability of drugs from eyedrops

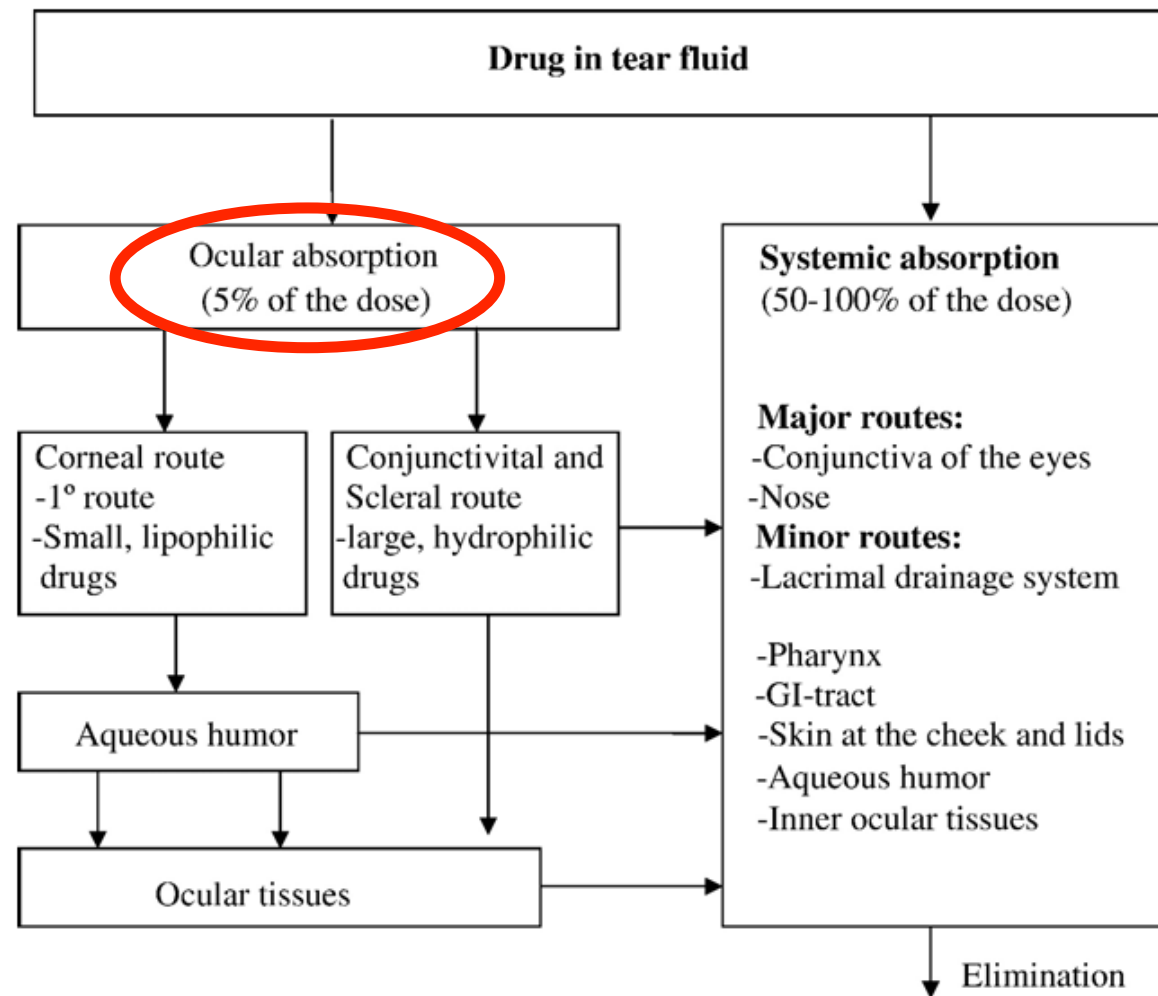
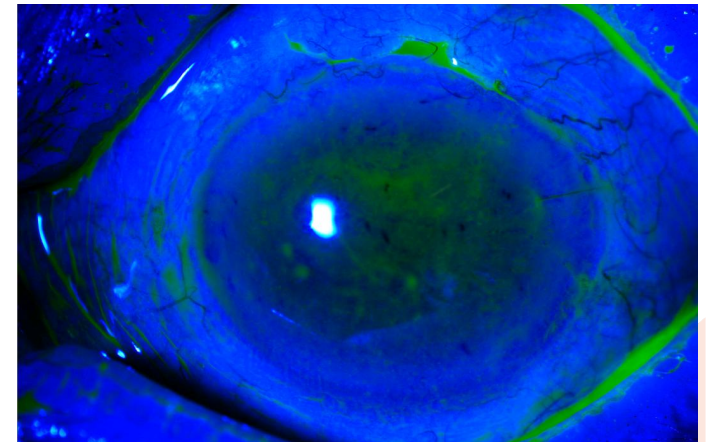
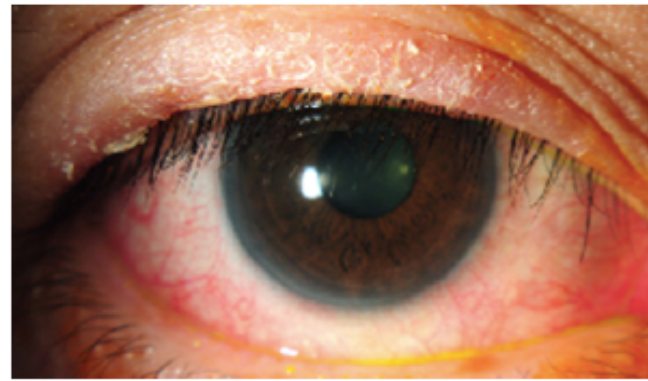
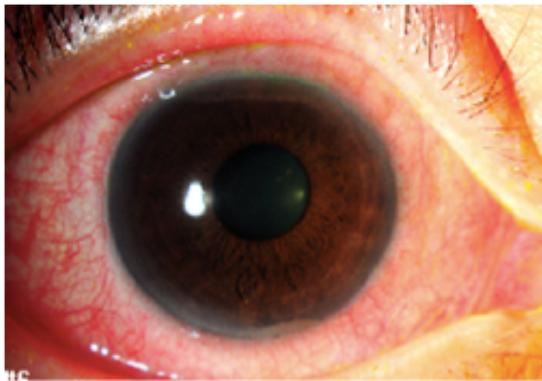


Fig. 2. Schematic diagram of ocular absorption.

Ocular surface disease and glaucoma

- Common problem
- Preservative induced OSD – non-compliance of 64%



Kulkarni SV, et al., Patient Prefer Adherence. 2008, 302-314

Glaucoma and Compliance

Patient compliance to medical treatment is an important factor in controlling glaucoma:

- ensures a constant daily IOP control
- at least 10% of glaucomatous visual loss is due to poor compliance
- >70% of glaucoma subjects stop therapy and/or prescription refill

(Ashburn et al. Surv Ophthalmol, 1980)

Glaucoma & Compliance

Total number of medications (frequency)

Appropriate application

Poor understanding of disease

Poor doctor-patient communication

Possible Solutions

Medications - *Patient dependent*

- more tolerable (change of preservative/ preservative free)
- easier to administer

Longer duration of action – *Patient non dependent*

=> sustained drug delivery/release

Chong et al. 74% acceptance of subconjunctival injection

3 monthly to replace eyedrops

Chong RS. J Glauc 2013:190-4

Features and benefits of sustained drug release

Advantages

- Efficient drug use – less wastage
- Drug effect independent of patient compliance
- Targeted delivery of drug to appropriate site – round the clock delivery

Benefits

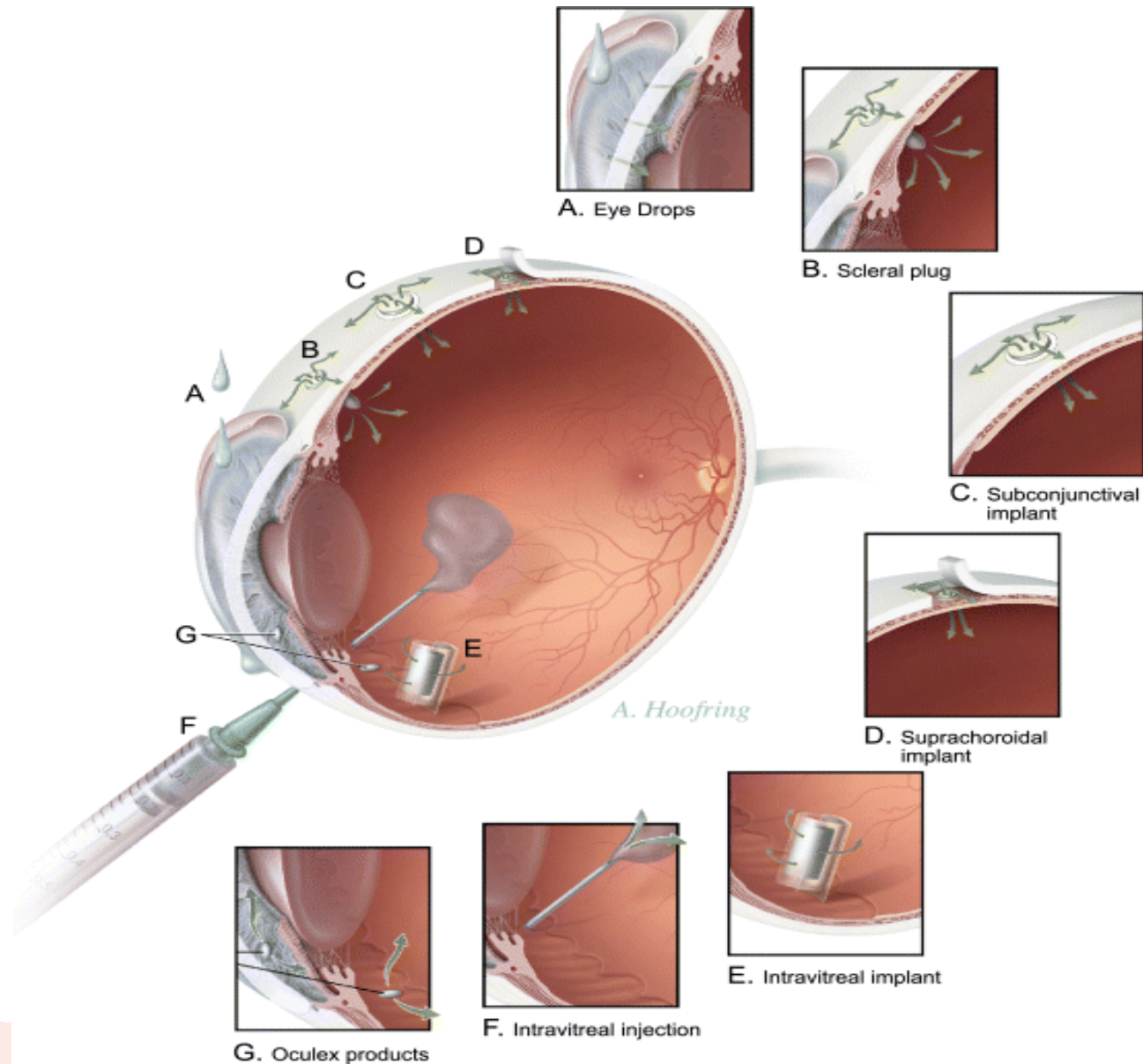
Patient

- Freedom from frequent eyedrops use
- Convenience/improvement on quality of life (fewer clinic visits)

Ophthalmologist

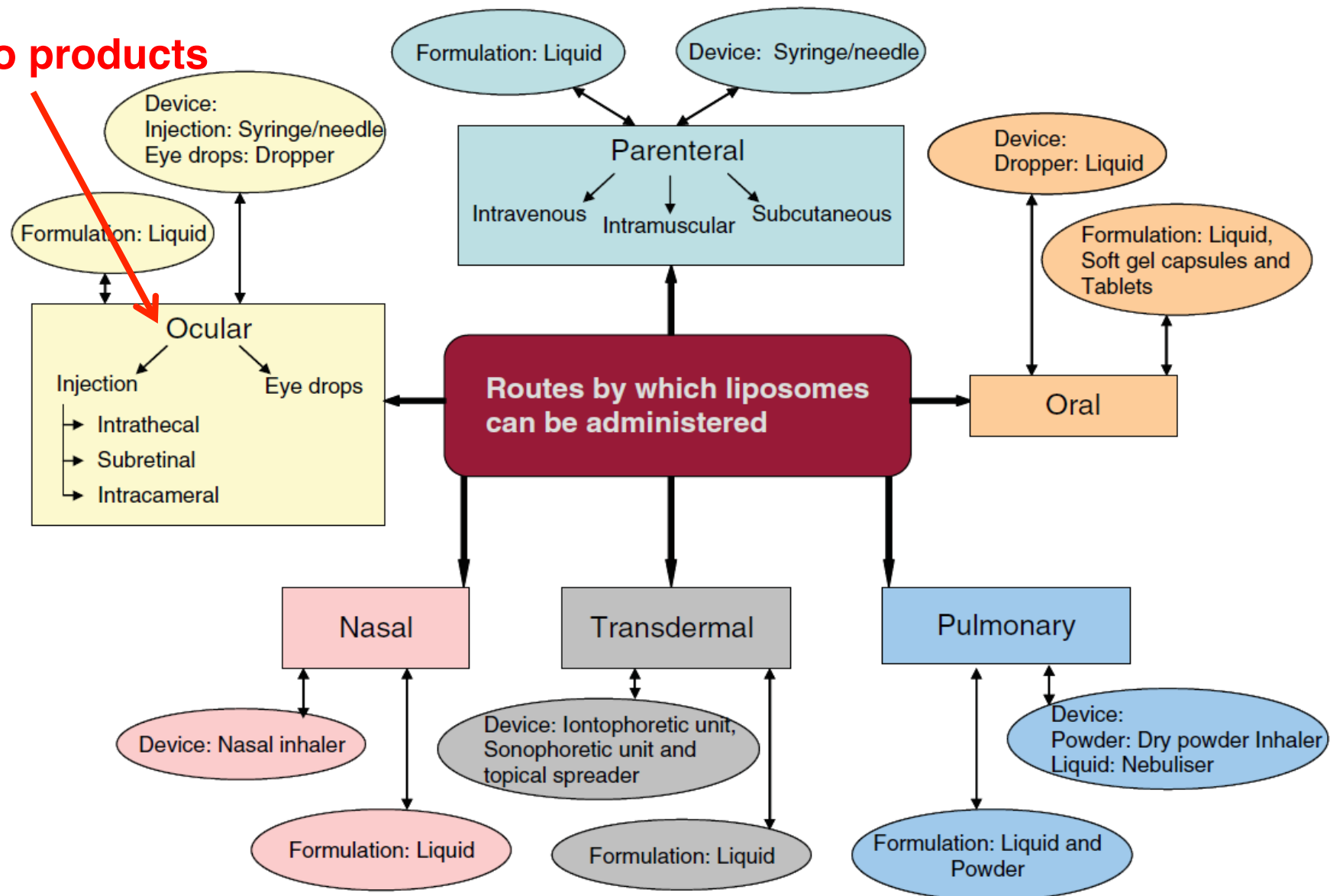
- Reassurance medication is being delivered

Routes for Targeted Ocular Drug Delivery



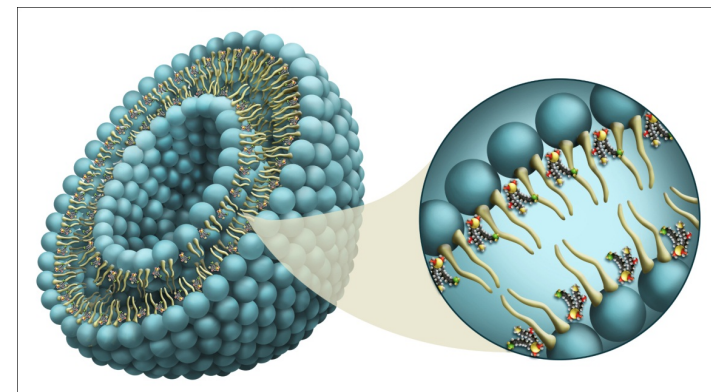
12 approved liposome based drugs, 25 in clinical trials

Zero products



The challenge: sustained release with nanoliposomes

- The focus is on using nanosize to enhance cellular penetration, or to enable prolonged circulation time in IV administration
- No nanocarrier drug product can sustain delivery of drug for more than 5 days
- Major challenges are of sufficient drug loading and of controlling release of loaded drug



Comparison of Xalatan and liposomal latanoprost

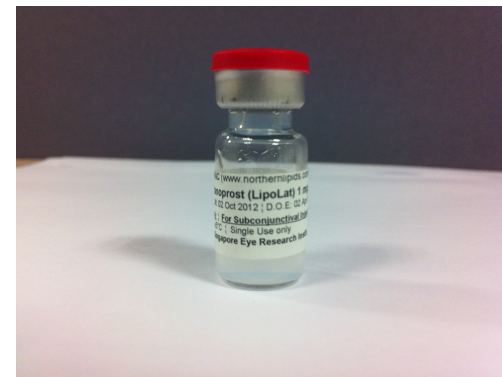
Xalatan

- 50ug/ml Latanoprost
- Lipid- Nil
- pH:6.5
- Preservative : Yes
- 0.02% Benzalkonium Cl

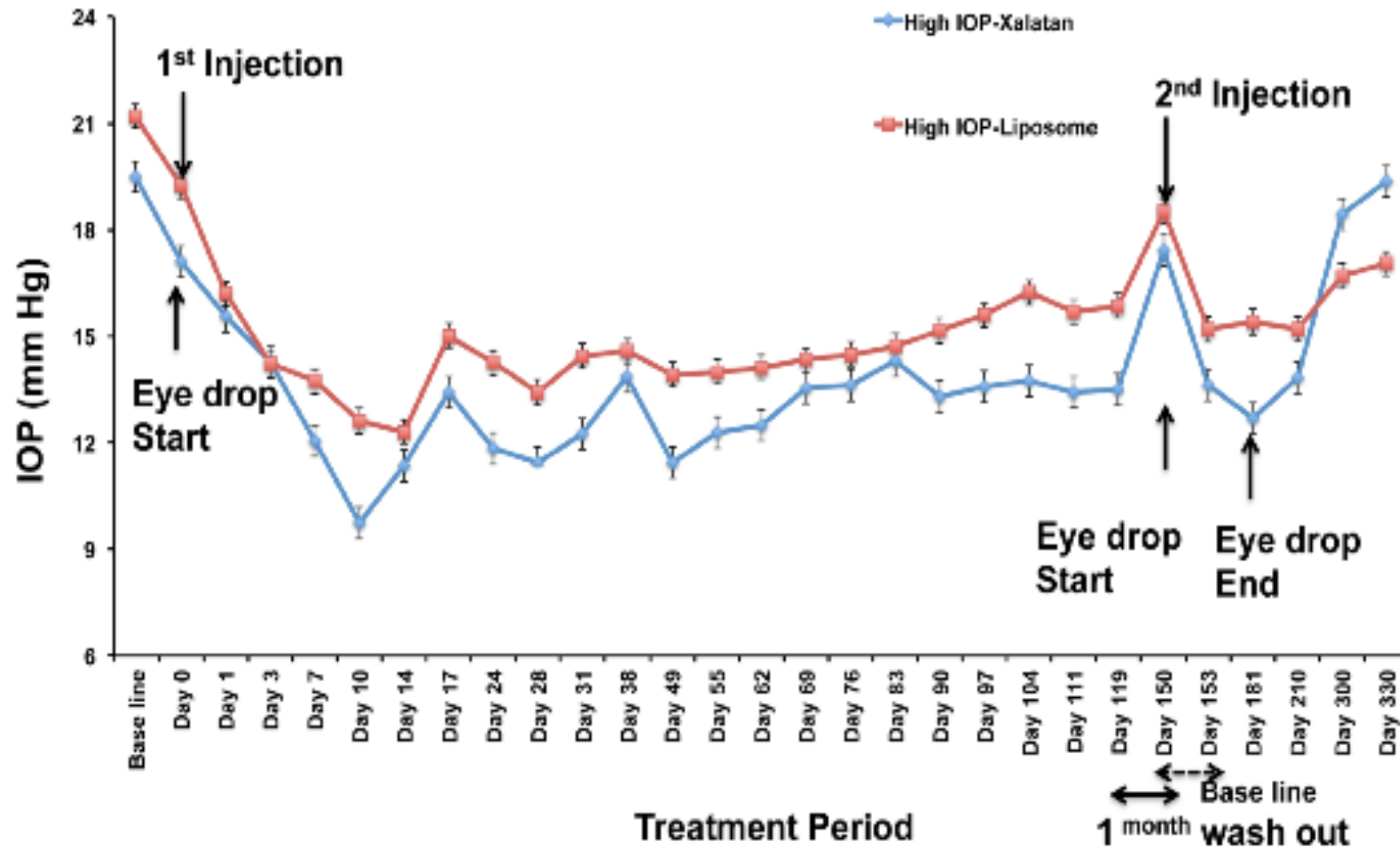


Liposomal Latanoprost

- 650ug/ml Latanoprost
- Neutral lipids
- pH:6.5
- Preservative : No



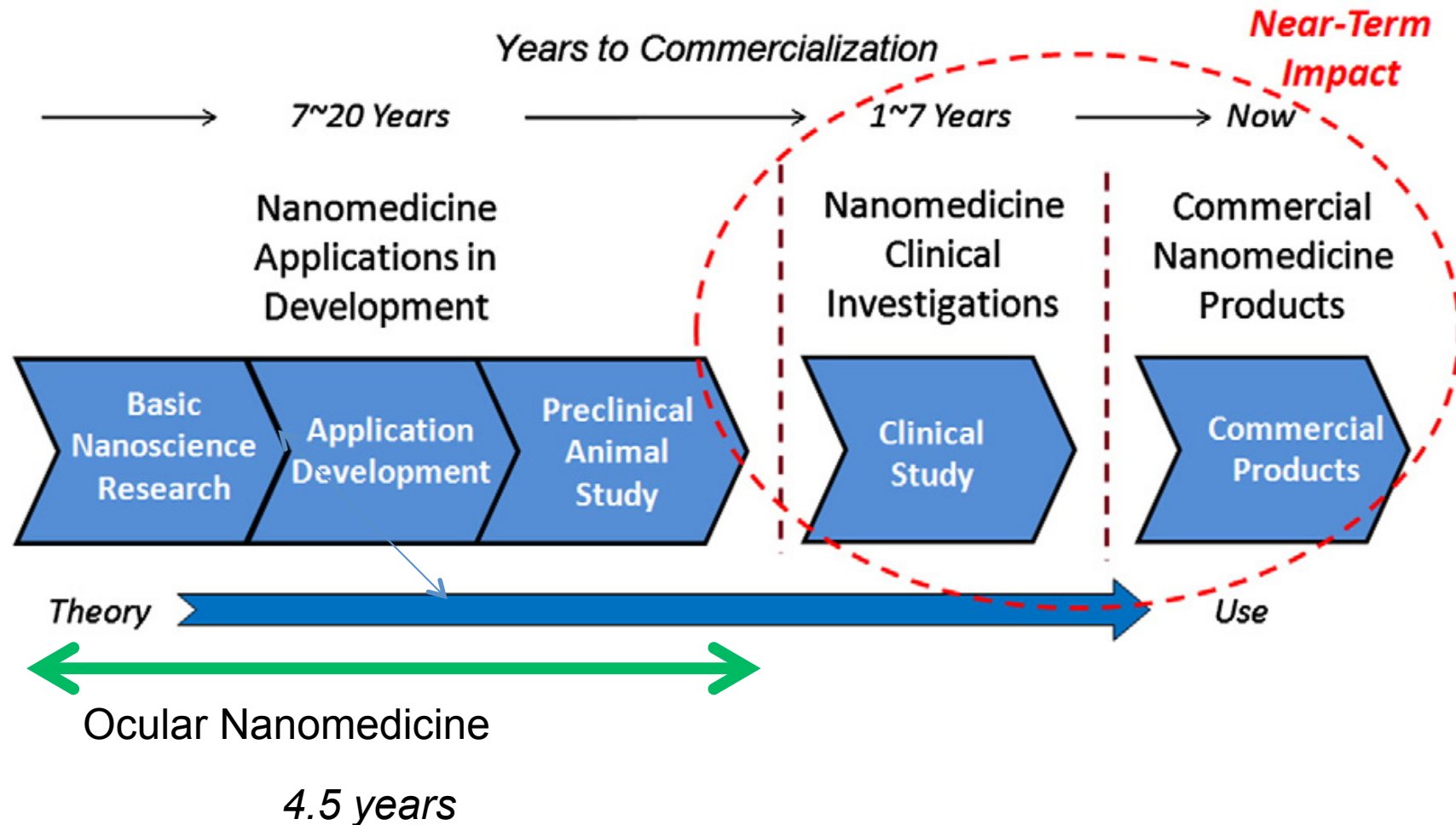
IOP response to Liposomal latanoprost in OHT Macaques



Natarajan JV, Wong TT, Venkatraman SS. 2014, 419-29 ACS Nano

Timescale of drug development

Nanomedicine Technology Development Pipeline



M.E.Etheridge et al, **The big picture on nanomedicine: the state of investigational and approved nanomedicine products**, *Nanomedicine: Nanotechnology, Biology and Medicine*, 9, pp1-14 (2013)

First in human trial
in Singapore

Clinical Trial Design

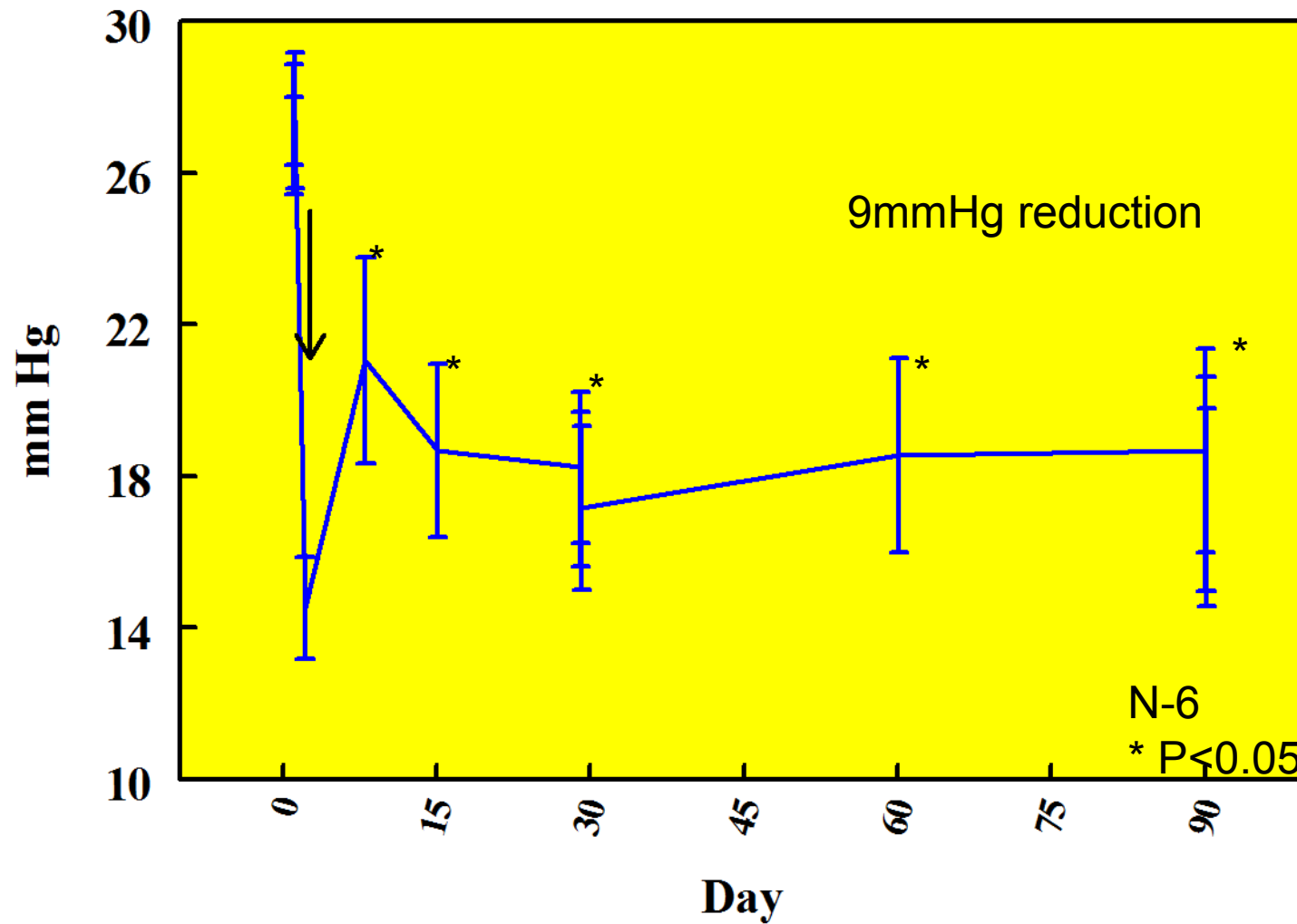
- Open label, single arm of 6 subjects
- Feb -July 2013
- Safety, feasibility and efficacy study
- 3 month study
- OHT or POAG
- Monotherapy

Clinical Trial Design

- Subconjunctival injection of 100uL liposomal latanoprost *
- IOP measured 1 hour post injection, 7 days, 14 days, month 1, 2, 3.
- Phasing performed at baseline D1 (day of liposomal latanoprost injection) months 1 and 3 at 0800, 1000, 1600hrs

* Injection performed after 1600hrs IOP measurement on Day 1 baseline phasing

>30% IOP reduction



Mean percentage IOP change from baseline

Visit	Time	Mean (SD)
Day 0	1700	-47.4 (10.1)
Day 8	0800	-24.6 (18.9)
Day 14	0800	-33.0 (15.7)
Day 28	0800	-34.4 (13.8)
	1000	-36.7 (12.0)
	1600	-38.5 (13.5)
Month 2	0800	-33.4 (18.6)
Month 3	0800	-33.3 (19.1)
	1000	-36.6 (20.0)
	1600	-38.9 (16.8)

Patient Tolerance

- Discomfort to subconjunctival injection (0/6)
- Ocular discomfort (1/6) - dry eyes – prescribed lubricants
- Redness (0/5)
- Pain/burning (0/5)
- Anterior chamber activity (0/6)

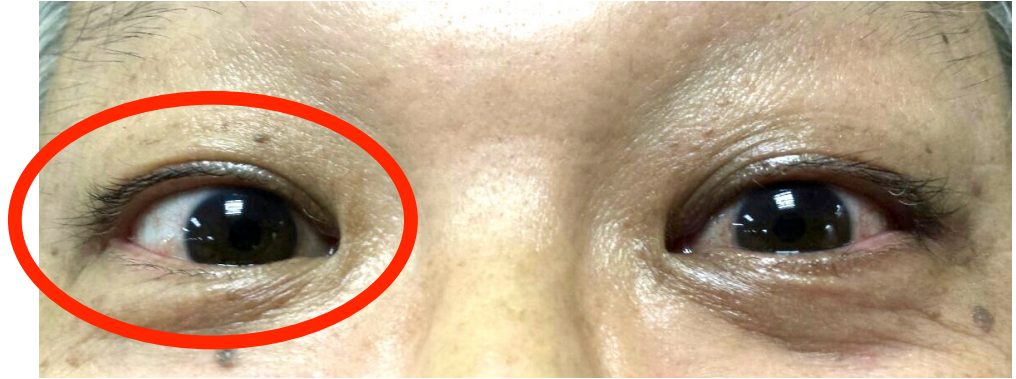
Subconjunctival Lipolat : Summary

- Liposomal latanoprost is the first sustained release nanomedicine developed for glaucoma
- It is well tolerated and without substantial safety issues
- 30% IOP reduction for >90 days

Patient Acceptance – No more red eye!!



pre-study baseline



post injection

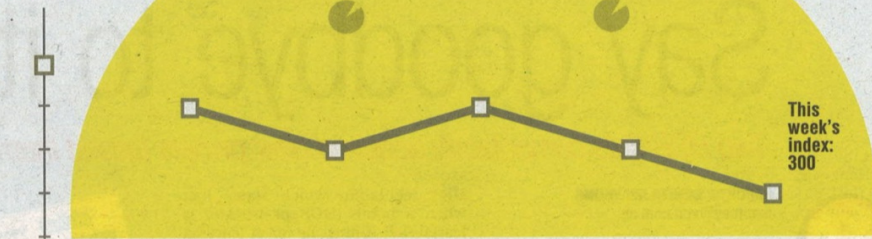


post injection

HAPPINESS INDEX

We rate the past week's news – good and bad

Last week's index: 330



Local maid agencies claim overseas counterparts sometimes increase the age of their maids to 23, the legal age to work

Just over 400 SingPass account passwords were reset without authorisation, revealed the Information

Nanyang Technological University and the Singapore Eye Research Institute developed a new treatment for glaucoma, which

The group, Action for Aids (Afa), said there has been a "worrying" rise in infections among homosexual men. The Ministry of

A survey by insurer AXA revealed that Singapore drivers feel less safe on the roads. The survey of 458 motorists found 62 per cent believed

联合早报 星期三 2014年6月4日

本地研发出世界第一款 治疗青光眼纳米眼药水 半年只须注射一次

名为“脂质体拉坦前列素滴眼液”的新纳米眼药水，化学成分与传统眼药水相同；不同的是，患者不必亲自滴这款眼药水，而是由医生代劳，新型眼药水中的脂质体会在下来六个月内，不断在眼球内部释放药物。这款眼药水料两年半内推出市场。

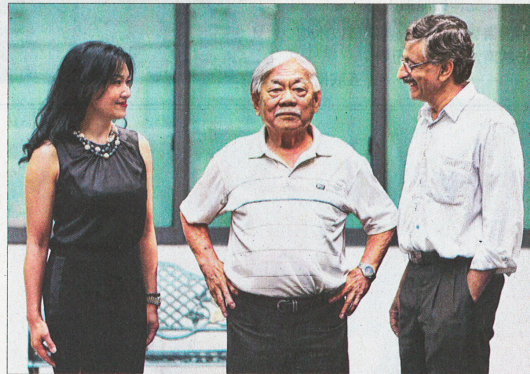
沈越 报道
sheny@sph.com.sg

本地科研人员研发出世界首款治疗青光眼的纳米眼药水，可使患者免受滴传统眼药水麻烦，也不必担心产生副作用。这种药物预计能在未来两年半内问世，届时将彻底改变现有的青光眼疗法。

液”（Liposomal latanoprost）的新型纳米眼药水，化学成分与传统眼药水相同。

不同的是，纳米眼药水的成分是装在体积极小的脂质体（liposome）中。脂质体具有与生物细胞膜类似的组织，能很好地与生物组织相容。

患者不必亲自滴这种眼药水，



青光眼科专家陈东江（中）去年初接受新型纳米眼药水的注射后，眼压有

First sustained release nanomedicine - a technological breakthrough

THE STRAITS TIMES

THURSDAY, JUNE 5, 2014

New treatment does away with daily eyedrops

By LINETTE LAI

EYEDROPS usually have to be applied daily for people with glaucoma, a disease which damages the optic nerves and can cause blindness. Yet this is something that the elderly, who make up the bulk of patients, tend to overlook.

A new nanomedicine could solve this problem.

In a new procedure expected to be offered commercially in future, glaucoma medicine in the form of millions of tiny capsules is injected into the eyeball.

These capsules slowly release their contents over six months, replacing the need for daily eyedrops that help relieve pressure on the optic nerve.

Performed under local anaesthetic, the procedure has so far been carried out on a trial group of six patients, doctors told reporters on Tuesday.

One of the patients is retired teacher Gordon Deans, 83, who has glaucoma in both eyes.

He had expected to feel some initial discomfort. "But it was absolutely painless," he recalled. "If the doctor didn't tell me it was over, I wouldn't have known."

The medicine was jointly developed by the Nanyang Technological University and the Singapore Eye Research Institute.

Clinical trials on a larger scale are on the cards before the treatment is offered commercially.

Scientists hope it will help prevent the worsening of glaucoma among the elderly here.

Many patients forget to apply eyedrops regularly or find it "too troublesome" to do so, said Associate Professor Tina Wong of the eye research institute.

"It is estimated that at least 10 per cent of blindness from glaucoma is directly caused by poor pa-

President's Technology Award 2014



**Academia
2008-2013**

**Private
2014-**



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**NANYANG
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Conception – Phase 1

NMRC funding

US Phase 2 – commercialisation

Angel Investor
Spring Singapore

Thank you

