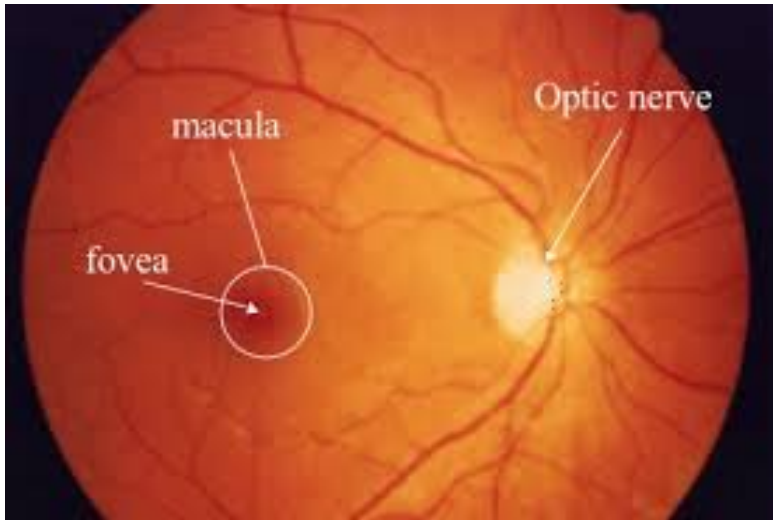
AURITEC Pharmaceuticals, Inc.

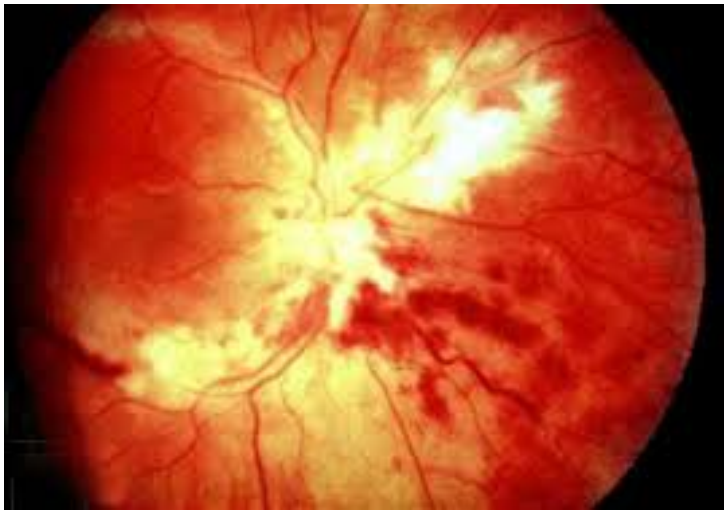
Intravitreal Sustained Release Ganciclovir: An Orphan Generic

25 Years of FDA History and the Future

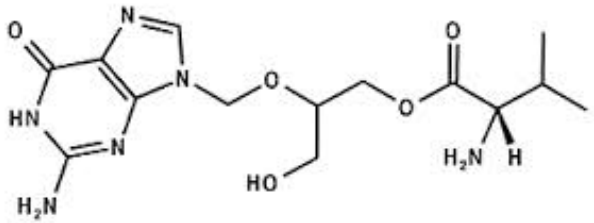
Thomas J Smith MD

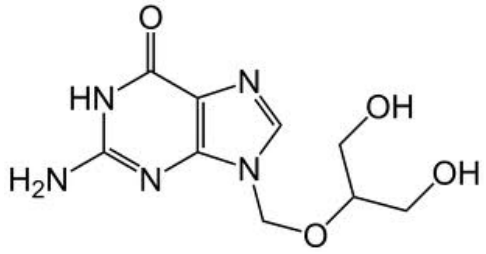
CMV Retinitis

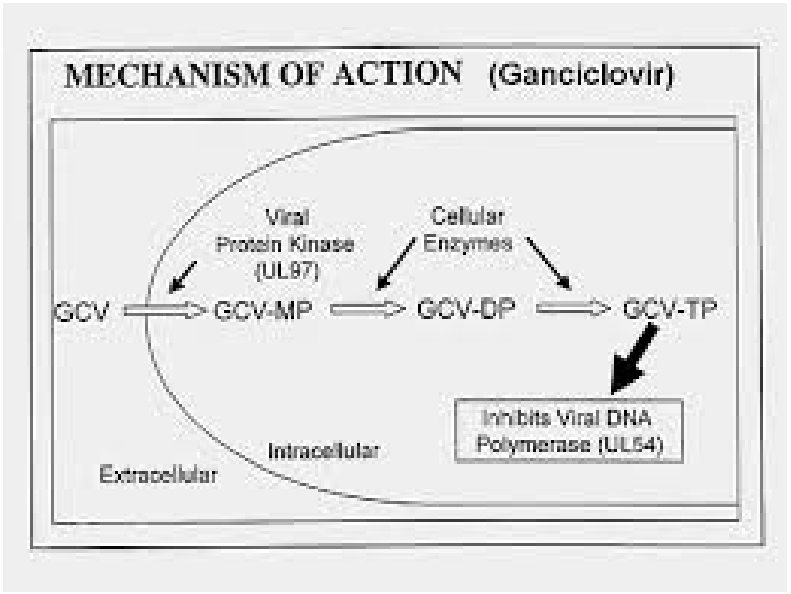




Ganciclovir

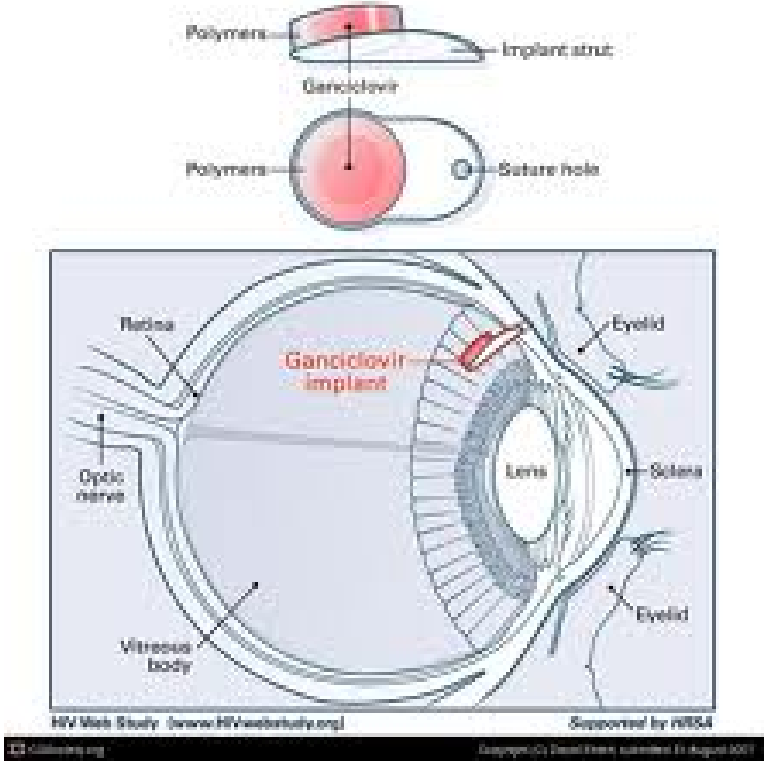


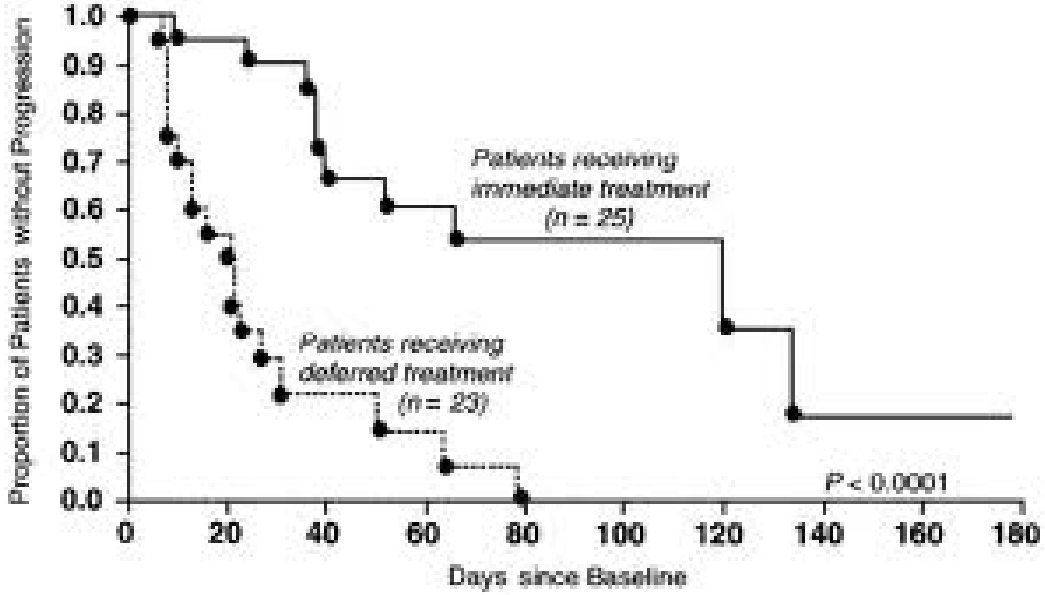


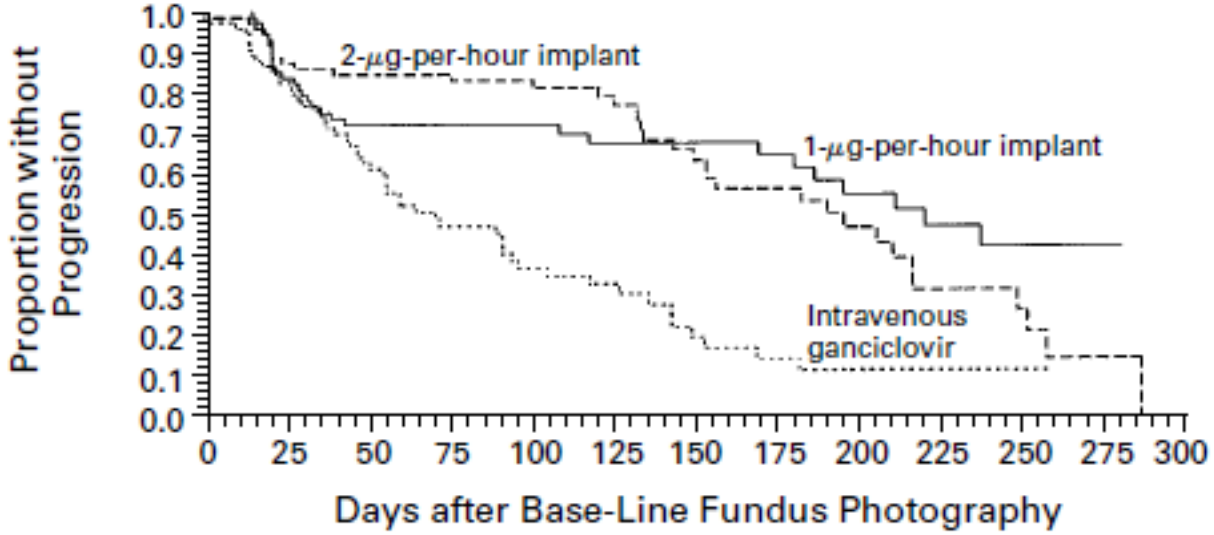


The Vitrasert

- NDA 020569 1995
- Early funding through ***FDA SBIR grant***
- University lab →
- Small Business →
- Biotech – Chiron →
- NDA →
- Bausch & Lomb




Proportion of Patients without Progression
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
Patients receiving immediate treatment (n = 25)
Patients receiving deferred treatment (n = 23)
P < 0.0001
0
20
40
60
80
100
120
140
160
180
Days since Baseline


Proportion without Progression
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
2-μg-per-hour implant
1-μg-per-hour implant
Intravenous ganciclovir
0
25
50
75
100
125
150
175
200
225
250
275
300
Days after Base-Line Fundus Photography

CMV Retinitis in the Age of HAART

Market insufficient to support Vitrasert

US: Incidence of 3.6 per 1000 PY

HIV prevalence 1M = 3600 cases per year

Alternative Rx – B&L discontinues Vitrasert 2013

ROW: Asia pooled prevalence 14%

– "Prevalence of CMV retinitis in resource low and middle-income countries, notably Asian countries, remains high" WHO CID 2013

OPEN ACCESS Freely available online

PLoS MEDICINE

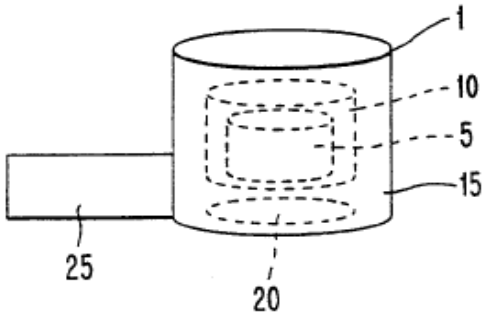
Neglected Diseases

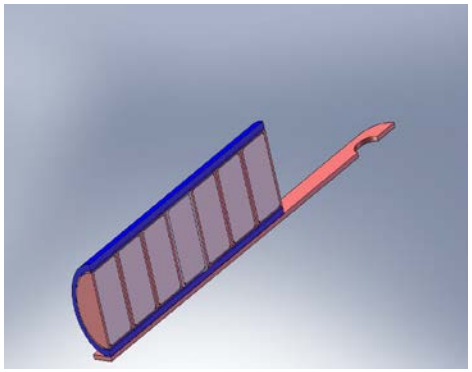
Cytomegalovirus Retinitis: The Neglected Disease of the AIDS Pandemic

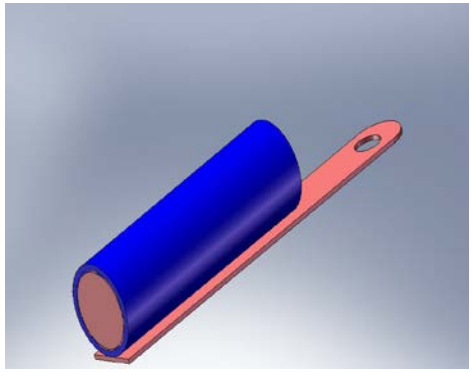
David Heiden*, Nathan Ford, David Wilson, William R. Rodriguez, Todd Margolis, Bart Janssens, Martha Bedelu, Nini Tun, Eric Goemaere, Peter Saranchuk, Kalpana Sabapathy, Frank Smithuis, Emmanuel Luyirika, W. Lawrence Drew

Generic Vitrasert

- ***FDA Grant U01 FD004927-01***
- GDUFA FY 2014 Research Priorities
  - Equivalence of Complex Products
  - Equivalence of Locally Acting Products
  - Therapeutic Equivalence Evaluation
- Q1/Q2
- Develop In vitro dissolution methods
- Match in vitro release
- In vivo bioequivalence







Challenges for ANDA

- Specific for Vitrasert
  - No predicate devices available
  - Clinical BE trials
    - Necessary?
    - Design?
    - Duration?
    - Crossover not possible
  - Super orphan in US – recruitment difficult
- For all Orphan Generics

The Problems with Orphan Generics

"You can't get there from here."

- Small market by definition
- Generic usually implies low price
- Products only a small company can love
- No investor, VC, or big pharma interest
- Less interesting for foundations (not malaria etc)

- No grant money including Orphan Drug Grants
  Q1/Q2 Generic = "not innovative"

Orphan Pull and Push Incentives

- Pull incentives:
  - market exclusivity provision
  - mechanisms to speed and facilitate review
- Push incentives:
  - tax credits,
  - consultation with staff on research designs,
  - exemption from user fees.
  - Orphan drug grants
- Generally Ineffective for Orphan Generics

The FDA – What We Do

FDA is responsible for advancing the public health by helping to speed innovations that make medicines more effective, safer, and more affordable.

http://www.fda.gov/aboutfda/whatwedo/default.htm

A Modest Proposal

Use GDUFA funds within the constraints of the legislation to promote orphan generic products, expanding existing orphan drug grant programs specifically to promote generic orphans