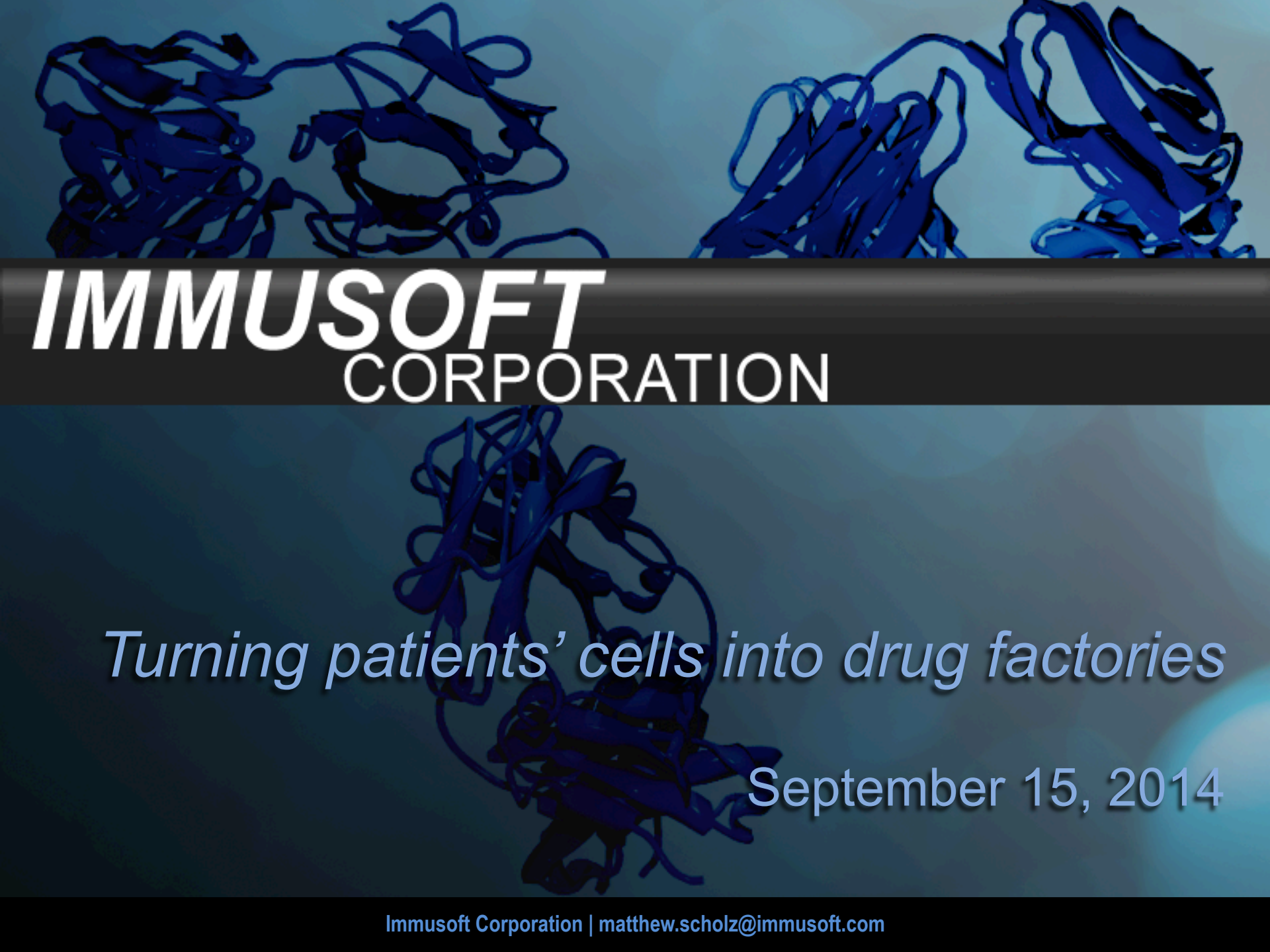


IMMUSOFT CORPORATION

Turning patients' cells into drug factories

September 15, 2014

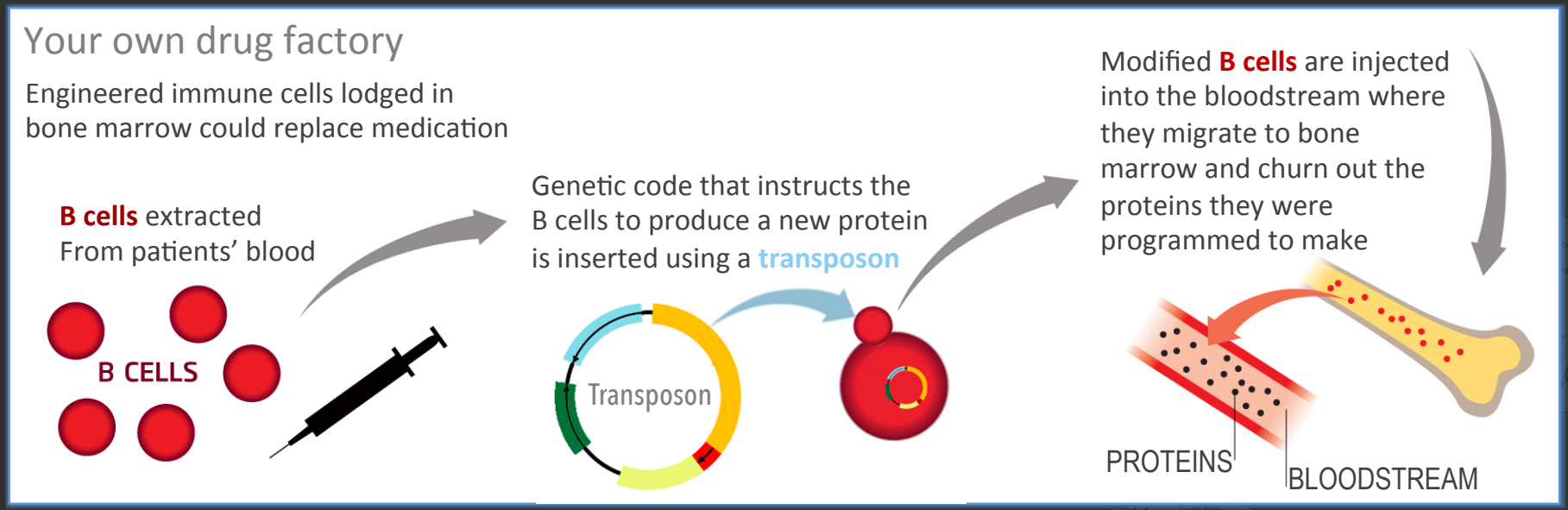
Immusoft Corporation | matthew.scholz@immusoft.com

IMMUSOFT: OVERVIEW

- Immusoft turns patients' cells into drug factories
  - *Ex vivo* cell therapy
  - Genomic modification of cells
  - Autologous long-lived plasma cells engraft and secrete therapeutic proteins *in vivo* for many years

IMMUSOFT: PROCESS OVERVIEW

Immusoft's Immune System Programming (ISP™) platform turns patients' cells into drug factories



Artwork adapted from New Scientist article about Immusoft
Issue 2935, 20 September, 2013; Mini drug factory churns out drugs from inside bone

BUSINESS STRATEGY
START SMALL THEN GO BIG

First Human Trials

MPS I (Hurler-Scheie syndrome)
- Rare genetic disease
- Very experienced collaborators
- Only a small amount of enzyme is needed
- Annual market value ~$219M

HIV
- Great patient advocacy groups
- Quick and clear efficacy data
- Market value > $9B in the US

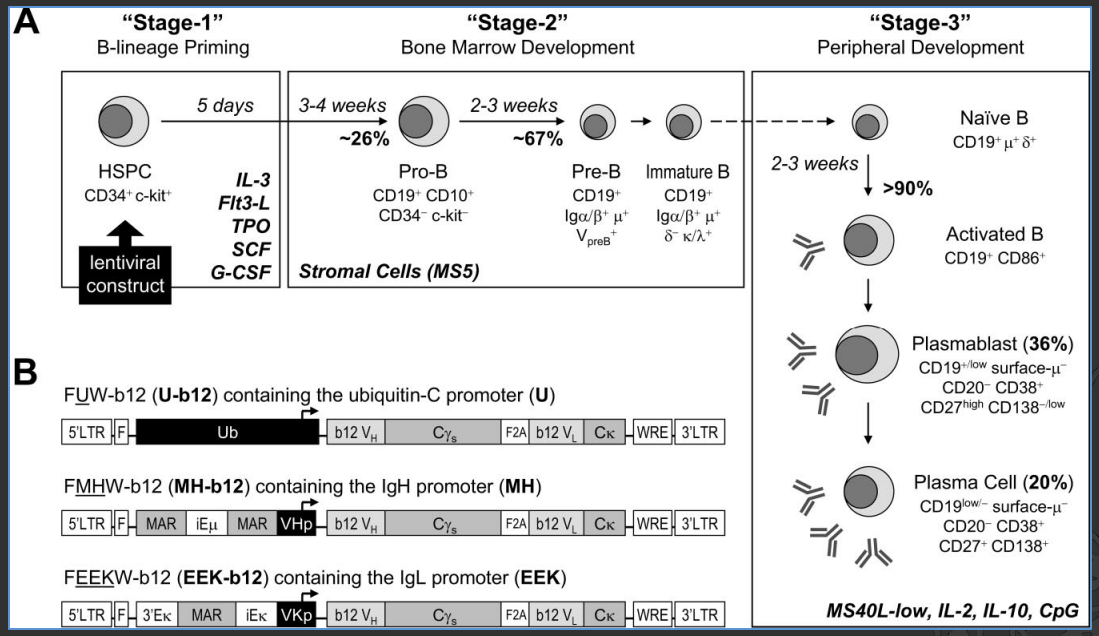
Commercial Focus

Rare diseases
- MPS I, Hemophilia A, LCAT deficiency Pompe, PKU
- Accelerated regulatory approval
- Will advance multiple indications at once
- $127B market by 2018

Heart disease
- Novel class of therapeutic in a > $100B market

SCIENTIFIC BACKGROUND

- Original IP from the Lab of David Baltimore at Caltech
  - Culture system for differentiating $CD34^+$ HSCs into plasma cells
  - Synthetic plasma cell-specific promoter (based on the kappa light chain promoter) drives protein expression

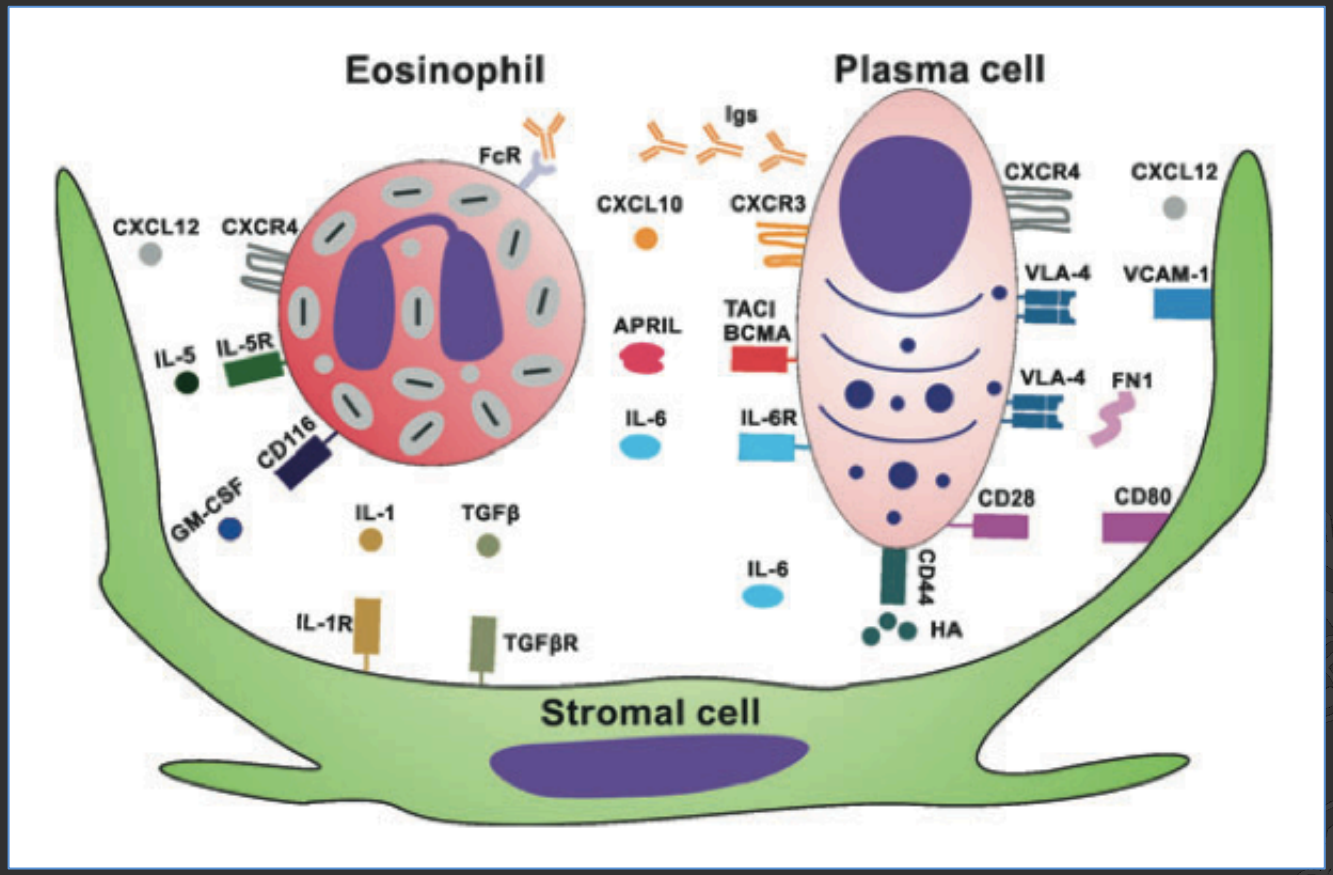


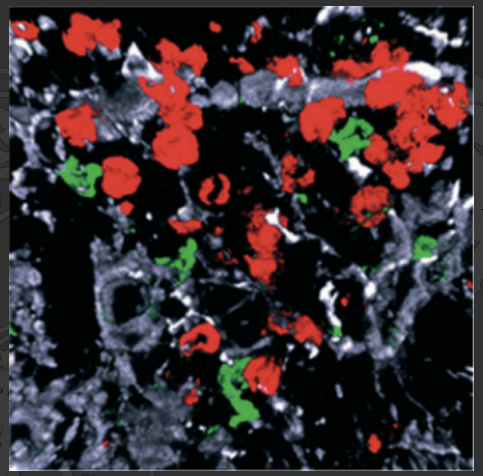
(Luo et al. 2009)

SCIENTIFIC BACKGROUND

- Immusoft modified the system to work with B cells isolated from peripheral blood
  - Memory B cells or naïve/resting B cells
  - Reduced the culture time from 10 weeks to 10 days
  - Initially by changing the pseudotype of the lentiviral vector
    - Using hemagglutinin and fusion proteins from the measles virus
    - This proved challenging to scale because of low viral titers 1-4 × 10^6 TU/mL
  - Later by modifying the culture system
    - Could use standard VSV-G lentivirus with titers of 2 × 10^7 - 1 × 10^8 TU/mL
  - Now working with transposons (non-viral vector)

BONE MARROW
SURVIVAL NICHE

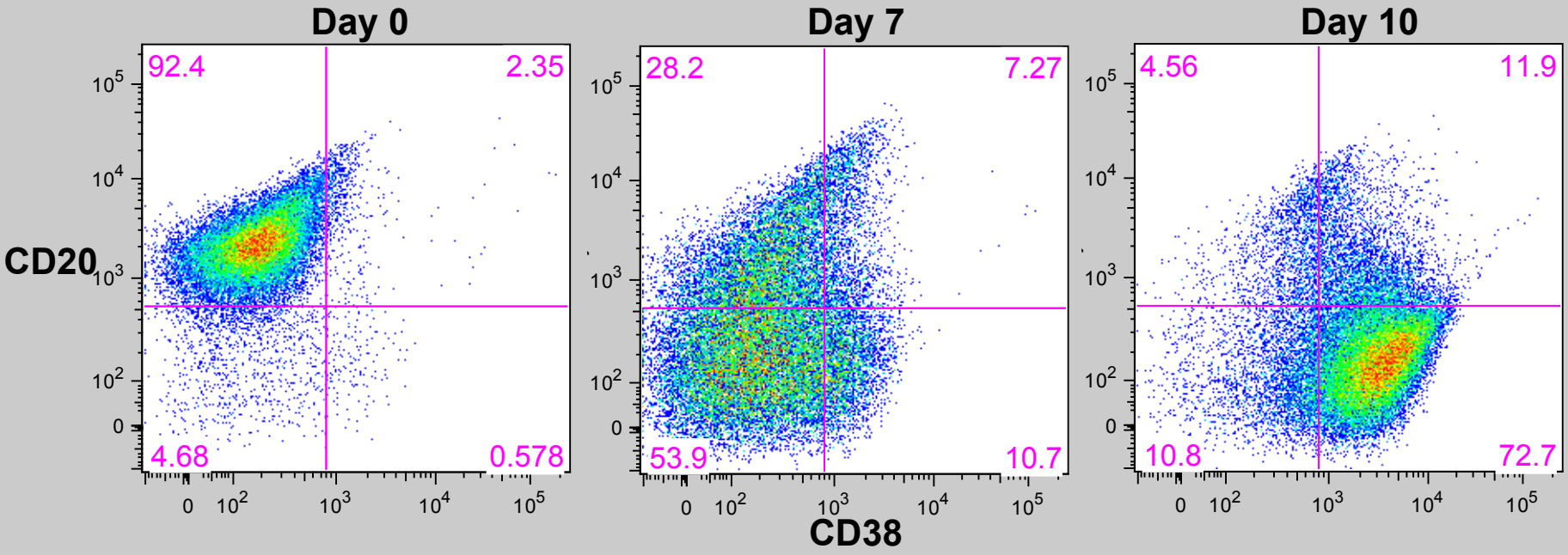




(Van T. Chu Claudia Berek 2013)

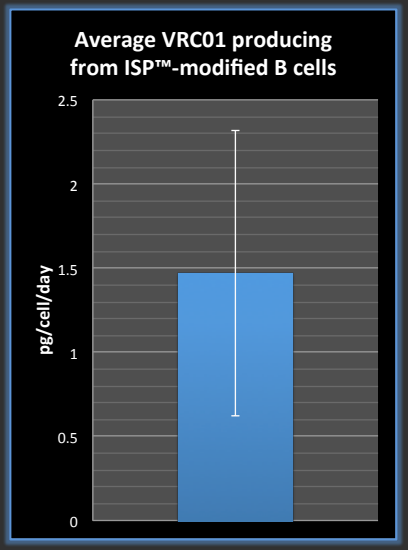
OPTIMIZED CULTURE SYSTEM

Differentiating peripheral blood B cells into plasmablasts *ex vivo*

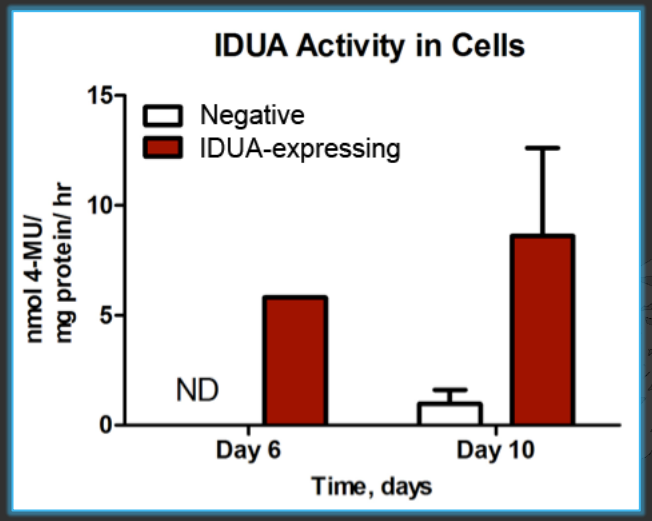


IN VITRO PROOF-OF-CONCEPT STUDIES

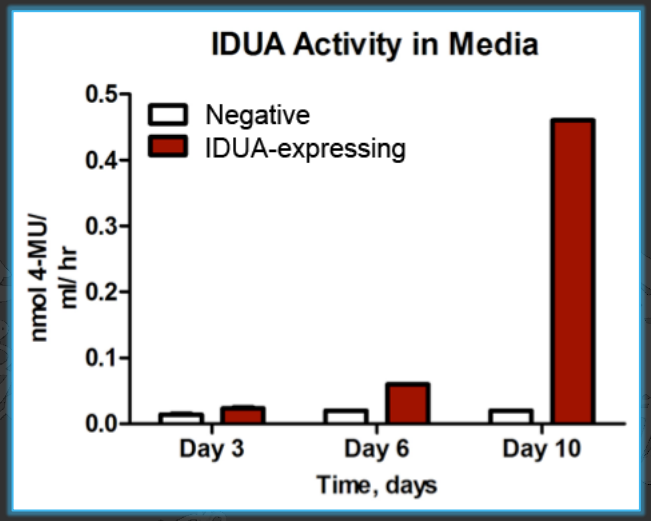
A clinically viable technology for programing patients' own immune cells to continually produce therapeutic proteins



B cells modified to produce VRC01, a broadly neutralizing antibody against HIV



B cells modified to produce the lysosomal enzyme α-L-iduronidase (IDUA) as detected by fluorometric assay in cell lysate

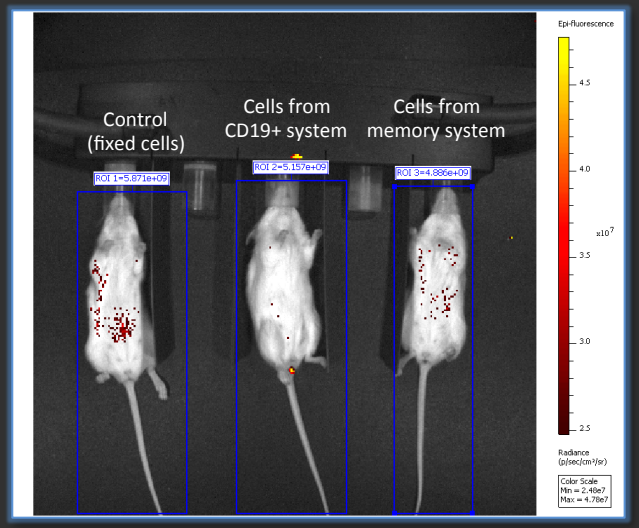


B cells modified to secrete the lysosomal enzyme α-L-iduronidase (IDUA) as detected by fluorometric assay in cell media

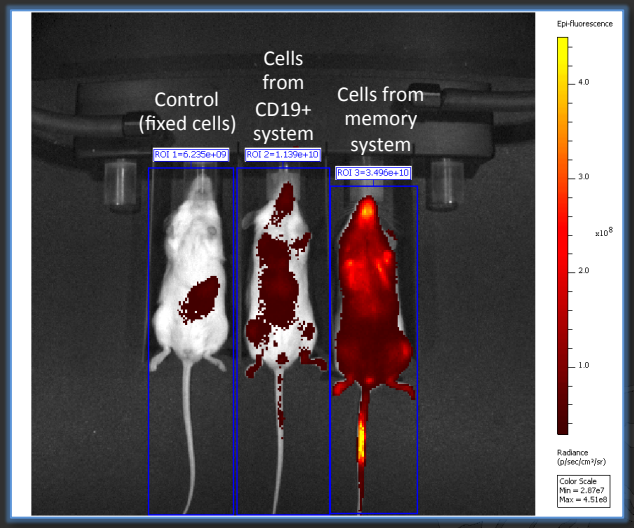
* The IDUA studies were performed in collaboration with Discovery Genomics

IN VIVO PROOF OF CONCEPT STUDIES

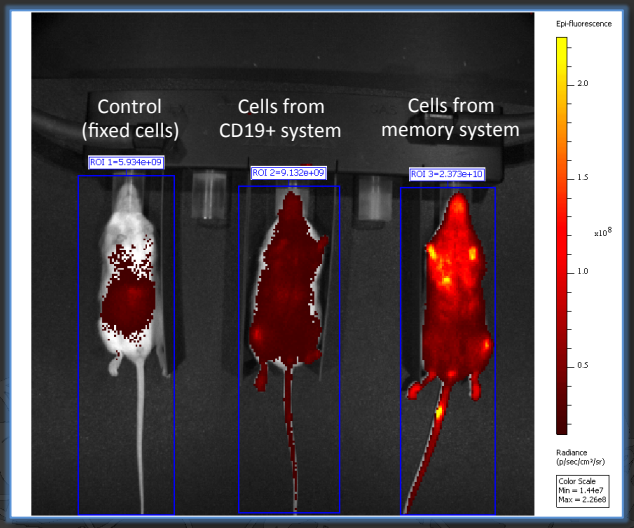
Plasmablasts migrating to survival niches in NSG mice



IVIS baseline signal (pre-injection)



IVIS signal 3 days post-injection



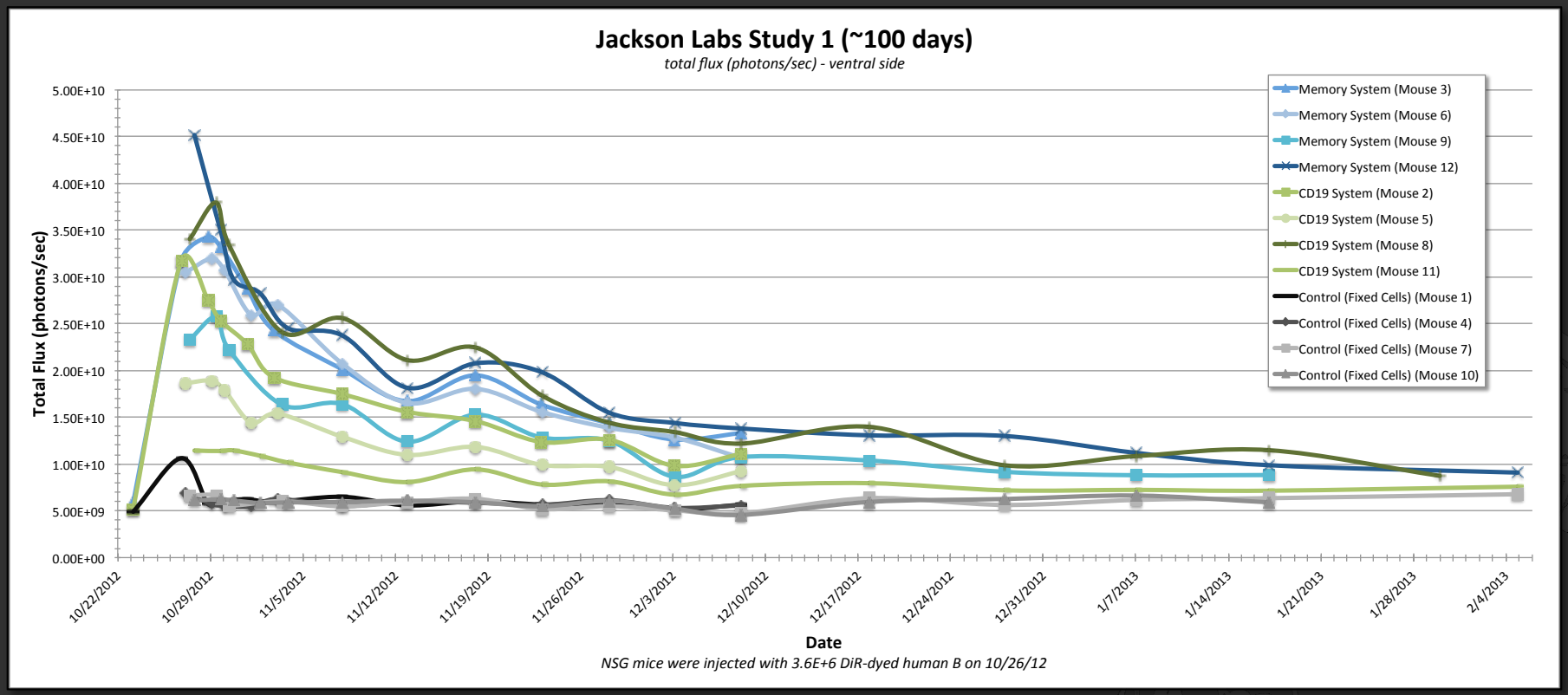
IVIS signal 11 days post-injection

** The half-life of long-lived plasma cells in humans is ~17 years*

The Jackson Laboratory
Leading the search for tomorrow's cures

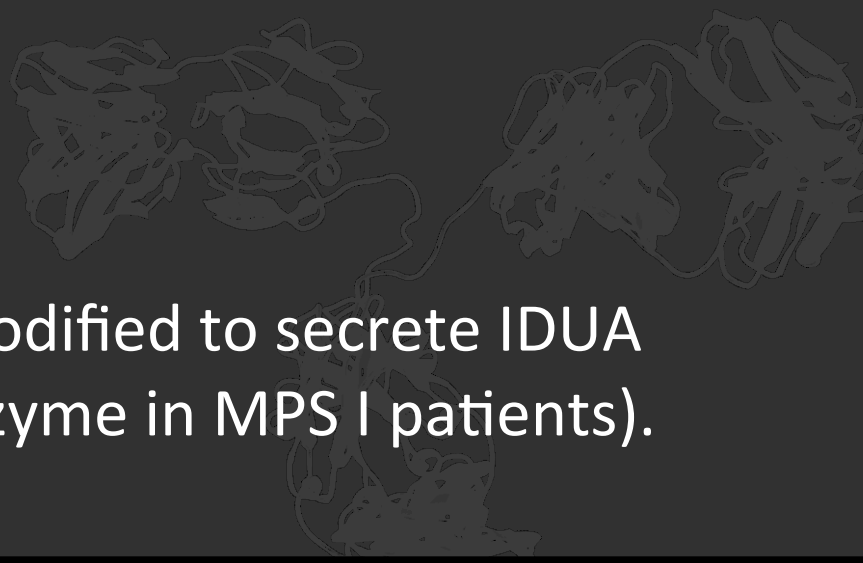
IN VIVO PROOF OF CONCEPT STUDIES

In vivo **imaging system (IVIS) data – signal from DiR dyed human B cells in mice**



CLINICAL TRIAL
MPS I

- To be performed at University of Minnesota (Investigator Sponsored Trial)
- Key collaborators
  - Paul Orchard, M.D.
  - R. Scott McIvor, Ph.D.
  - Perry Hackett, Ph.D.
- Treatment
  - Autologous plasmablasts modified to secrete IDUA (the missing or deficient enzyme in MPS I patients).



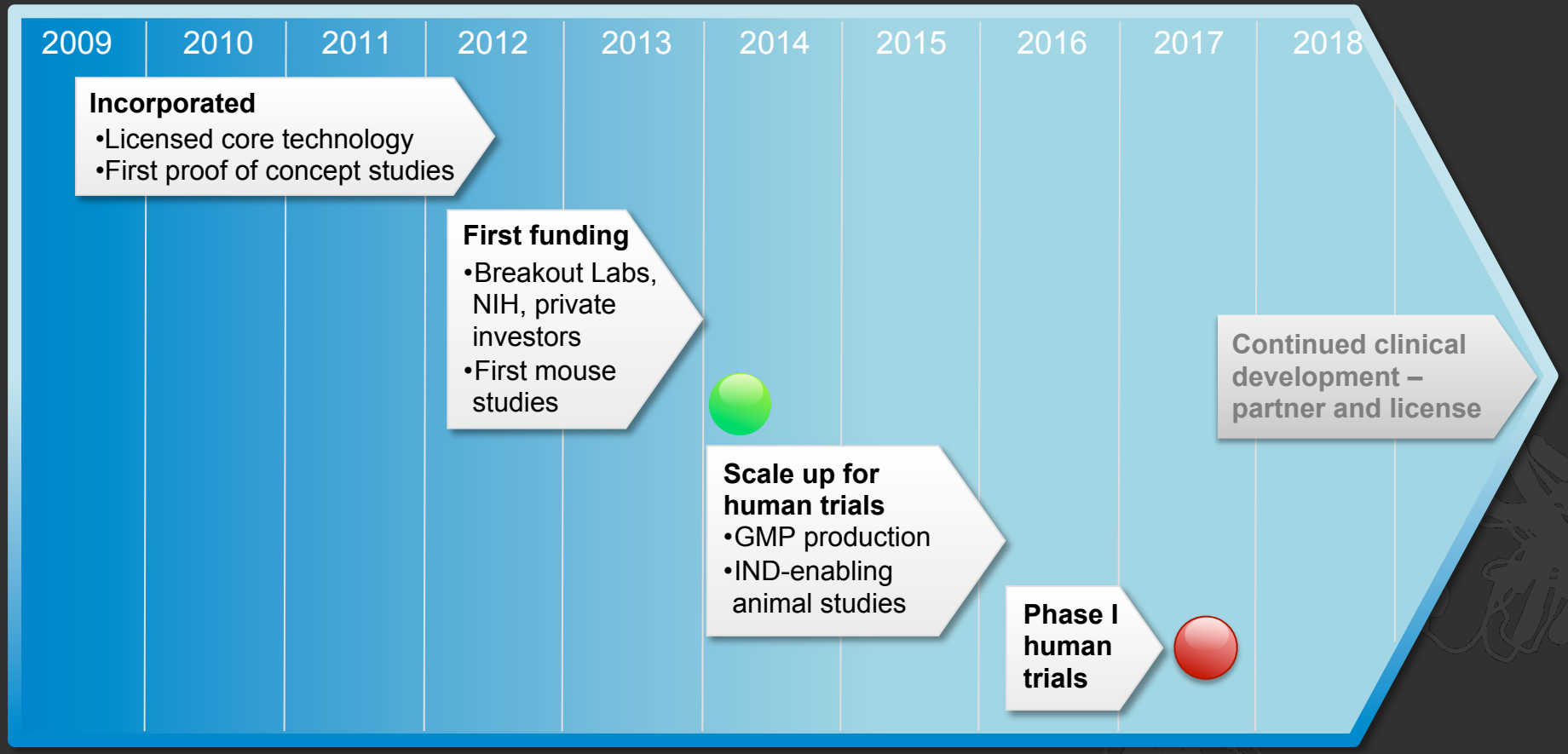
CLINICAL TRIAL
MPS I

- First informal interaction with FDA next week
- Pre-pre-IND meeting in ~3 months
- Proposed trial design
  - Multi-dose Phase I/II study
  - Rapid dose escalation (3 patient cohort)
  - Estimated therapeutic dose (6 patient cohort)
  - Four doses 2-4 weeks apart
- Proposed patient inclusion criteria
  - Prior allogeneic transplant >2 years previously
  - Age at enrollment <14 years
  - >10% engrafted based on recent testing
  - Willing to commit to traveling to the University of Minnesota every 6 months for the duration of the study
- Estimated start date Q1 2016

CLINICAL TRIAL
HIV

- To be performed at UCSF (Investigator Sponsored Trial) with collaborators:
  - Steven G. Deeks, M.D.
  - Galit Alter, Ph.D. – The Ragon Institute of MGH, MIT and Harvard
- Patient population
  - Treated with ART during acute/recent infection
  - Stable ART regimen for at least three years
  - Viral load < 50 copies/mL for last three years
  - $CD4^+$ T cell count > 500 cells/mm^3
- Treatment
  - Autologous plasmablasts modified to secrete a cocktail of broadly-neutralizing antibodies (Abs) against HIV targeting the long-lived viral reservoir.
  - If target Ab levels are maintained, patients will undergo scheduled interruption of ART.
- A collaborative $7M U19 grant application has submitted for this trial and its preclinical development.

TIMELINE OVERVIEW
PARTNER EARLY



- Fundraising for scale up and Phase I clinical trial
- First expected exit or licensing opportunity.

CORE TEAM AND COLLABORATORS

Immusoft

Mark Ahn, Ph.D.

Eric Garcia

Zach Hall

Eric Herbig, Ph.D., M.B.A.

R. Scott McIvor, Ph.D.

Matthew Scholz

Mei Xu, Ph.D.

Key Advisors and Collaborators

Steven Deeks, M.D.

Iqbal S. Grewal, Ph.D.

Shelly Heimfeld, Ph.D.

Daniel F. Hoth, M.D.

Hans-Peter Kiem, M.D.

Xin Luo, Ph.D.

Joyce Frey-Vasconcells, Ph.D.

Funding

FF Science

Grants

Private investors

Breakout Labs
A Project of the Thiel Foundation

NATIONAL INSTITUTES OF HEALTH

DGI DISCOVERY GENOMICS, INC.

Seattle BioMed

The Jackson Laboratory
Leading the search for tomorrow's cures

sfgh

FRED HUTCHINSON CANCER RESEARCH CENTER
A LIFE OF SCIENCE

Caltech

IMMUSOFT:
A NEW MEDICAL PARADIGM

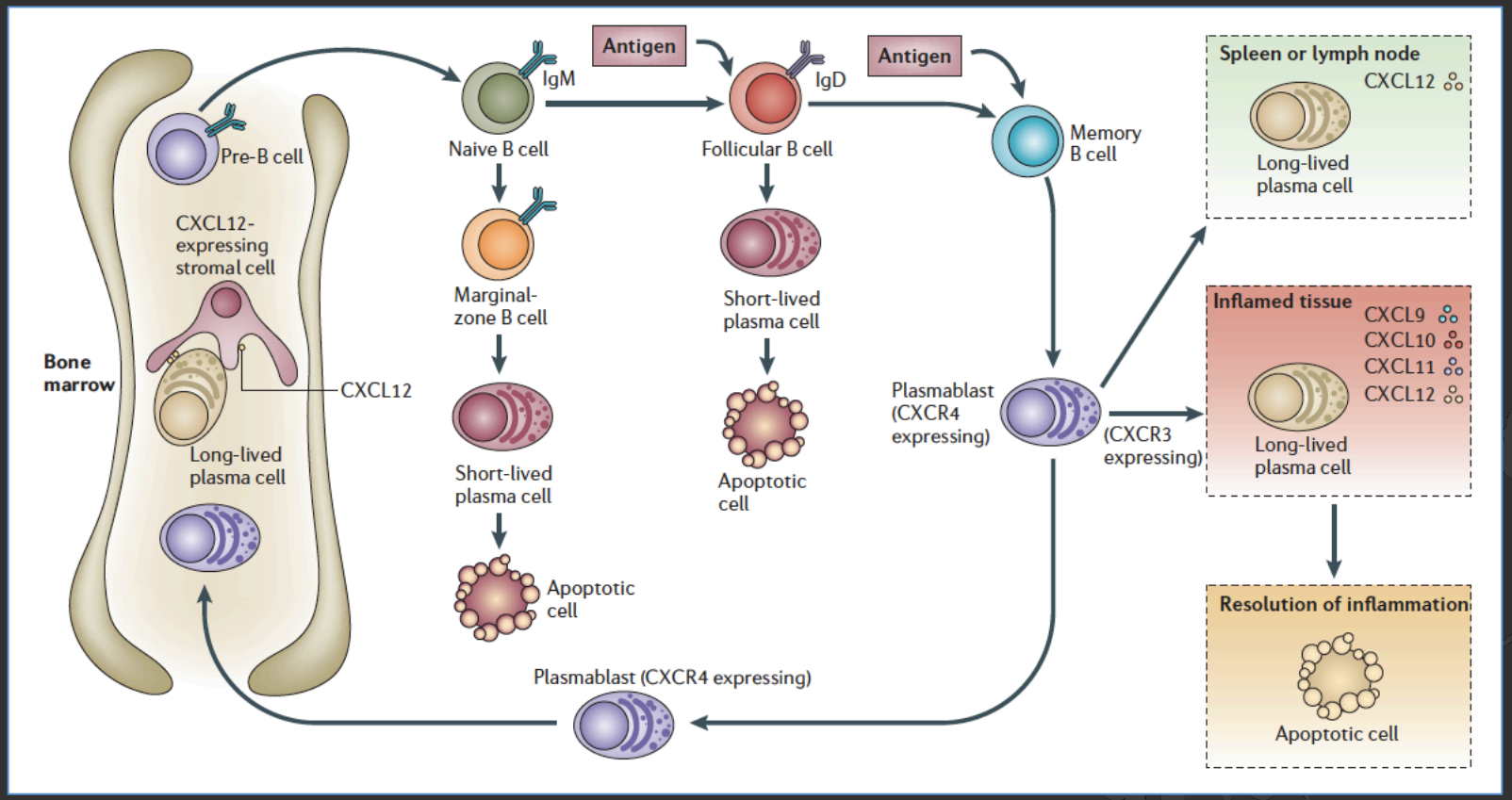
TURNING PATIENTS' CELLS INTO DRUG FACTORIES

matthew.scholz@immusoft.com

IMMUSOFT:
A NEW MEDICAL PARADIGM

SUPPORTING SLIDES

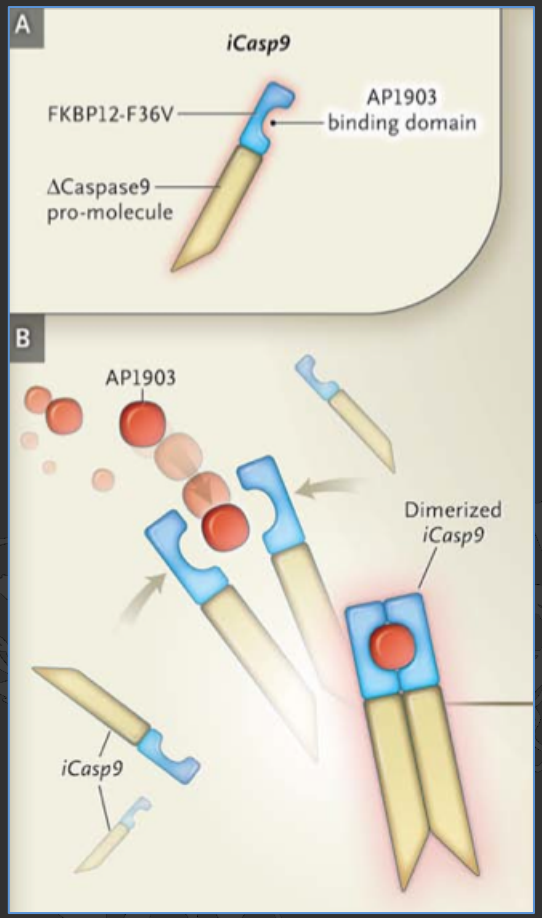
B CELL DEVELOPMENT AND MIGRATION



(Radbruch et al. 2006)

SAFETY FEATURES

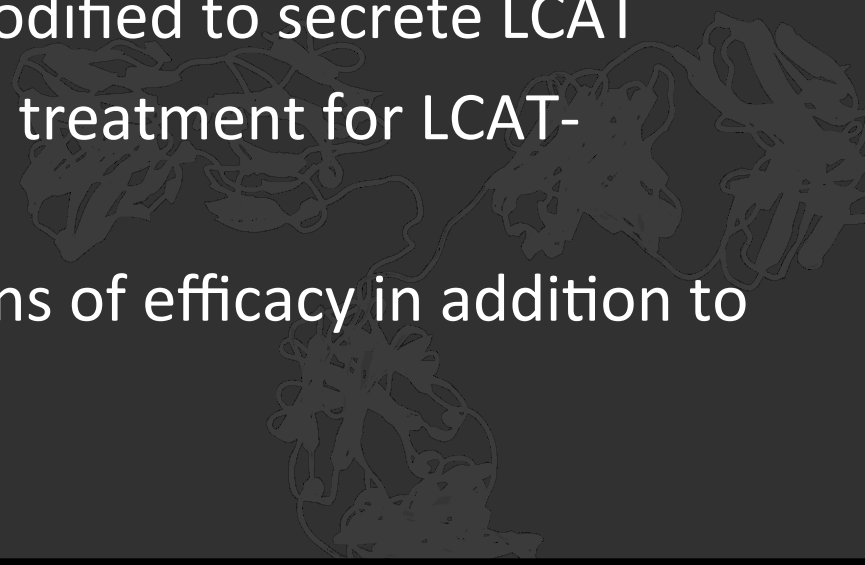
- Terminally differentiated cells instead of progenitor cells
- Inducible caspase 9-based suicide gene
  - Allows the rapid elimination of ISP™-modified cells with a chemical inducer of dimerization
  - Already used in humans
    - Killed more than 90% of the transduced cells within 30 minutes



(Di Stasi et al. 2011)

CLINICAL TRIAL
LCAT DEFICIENCY

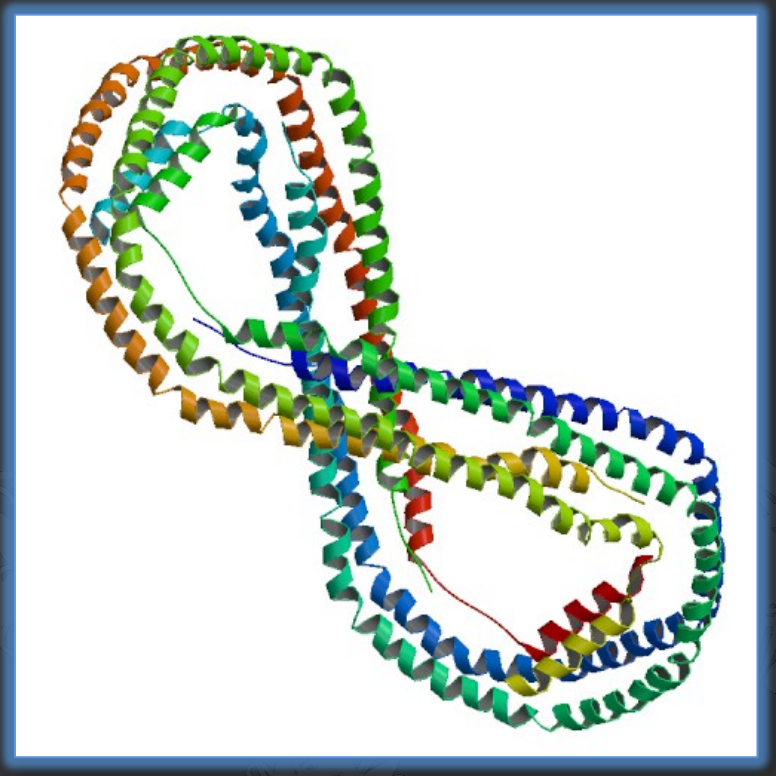
- To be performed at NHLBI in Bethesda, MD (Investigator Sponsored Trial) with collaborator
  - **Alan Remaley, M.D., Ph.D.**
- Treatment
  - Autologous plasmablasts modified to secrete LCAT
  - There is no approved causal treatment for LCAT-deficiency
  - Study should show clear signs of efficacy in addition to safety



HEALTH EXTENSION APPLICATIONS

ApoA-I Milano

- Discovered 30 years ago
- Clinical trial 15 years ago
- 123 patient Phase II
- Reduction in arterial plaque in 5 weeks
- Acquired by Pfizer for $1.3B
- Produce with ISP™ technology



Tissue Regeneration

- Transient p21 or CTGF suppression for tissue regeneration

COMPETITION AND ECOSYSTEM

Competition

- The old way (ERT)
  - BioMarin/Genzyme/Sanofi
  - Gilead (HIV)
- *In vivo* gene therapy
  - Genzyme/BioMarin (AAV)
  - Moderna/AstraZeneca (RNA)
- Ex vivo gene therapy
  - Bluebird Bio/Lentigen
  - Sangamo/Medimmune (HIV)

Not competitive but relevant

- CAR T cell treatments (cancer)
  - Novartis (U-Penn)
  - M.D. Anderson
  - Celgene/Bluebird Bio (Baylor)
  - Juno Therapeutics (St. Jude) (just raised $300M)
- Future technology
  - CRISPRs and TALENs
  - Nanoparticles

COMPETITION
AAV VECTORS

Advantages of ISP™ over adeno-associated virus (AAV) gene therapies

- AAV has a relatively small payload capacity
  - Can't effectively deliver whole antibody constructs or larger proteins
- ISP™ can incorporate a suicide gene system
- Plasma cells produce high levels of protein
  - AAV vectors don't effectively transduce B cells
- Our *Ex vivo* use of vector allows for multiple treatments without immune rejection
- AAV treatments will require ~5×10^{13} - 2×10^{14} viral genomes per dose. This is expensive!

BUDGET AND TIMELINE
PRE-CLINICAL TO PHASE I