UCSF Startups and Innovation in

Therapeutics

153 Therapeutics

NURR1 receptor modulators for the treatment of Parkinson's disease

Pamela England, PhD
Co-founder, 153 Therapeutics
UCSF Professor,
Pharmaceutical Chemistry

Matthew Jacobson, PhD
Co-founder, 153 Therapeutics
UCSF Professor,
Pharmaceutical Chemistry

10M Patients with Parkinson's globally (1M US), est. 90,000 new cases in the US each year

$5B Worldwide market for PD medications, projected to grow to $11.5B by 2029

100% All physicians surveyed would prescribe a neuroprotective therapy if available

DISEASE/INDICATION: Parkinson's disease (PD)

UNMET NEED:

- Current PD therapeutics are symptom-modifying only and lose efficacy with disease progression
- Novel therapeutics that treat PD symptoms and slow disease progression will be game-changers in the therapeutic landscape

PRODUCT: Small molecule neuroprotective therapy that modulates Nurr1 function

- Preclinical studies: compounds activate Nurr1, cross the BBB
- Published animal studies: activating Nurr1 repairs neurodegeneration

COMPETITIVE ADVANTAGE/DIFFERENTIATION:

- Potential for dual approach (symptom management + neuroprotection

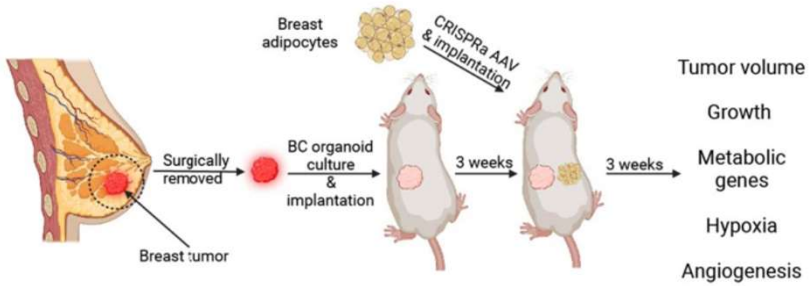
DATA/PROGRESS TO DATE:

- IP filed for composition of matter; IND-enabling work targeted for H2-2024

Adipose Manipulation Transplantation, A Novel Cancer Therapy

Nadav Ahituv, PhD

UCSF Co-Inventor
Professor, Bioengineering & Therapeutic Sciences Director, Institute for Human Genetics
Co-founder of Regel Therapeutics ($EFTR)



https://pubmed.ncbi.nlm.nih.gov/37034710/

DISEASE/INDICATION: Pancreatic ductal adenocarcinoma, breast cancer, and other cancer types.

UNMET NEED: Deregulated cellular metabolism, also known as reprogrammed metabolism, is a hallmark of cancer. There are some efforts to target cancer glucose and fatty acid metabolism for therapeutic purposes. However, there are currently no FDA-approved cancer treatments targeting lipid metabolism.

PRODUCT: CRISPRa Engineering white adipose organoids or adipocytes into brown fat, which is customized for different cancer-associated metabolic programs.

COMPETITIVE ADVANTAGE/DIFFERENTIATION:

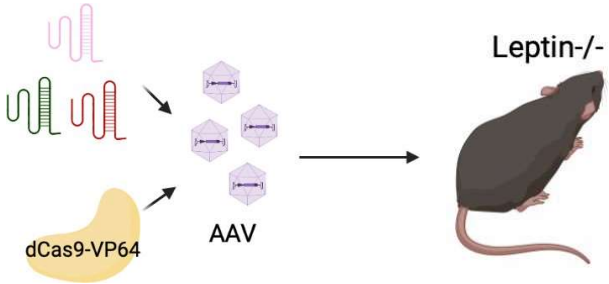
- Adiocytes have a lower immune response, allowing more straightforward development of “off-the-shelf” adipocytes.
- Removing and grafting fat are safe clinical procedures.

DATA: Proof of Principle results in xenograft models of pancreatic cancer and breast cancer.

Adipose Manipulation Transplantation, a Novel Therapy for Obesity Related Metabolic Disease

Nadav Ahituv, PhD

Professor, Bioengineering & Therapeutic Sciences Director, Institute for Human Genetics
Co-founder of Regel Therapeutics ($EFTR)



DISEASE/INDICATION: Metabolic diseases such as obesity and diabetes.

UNMET NEED: The prevalence of obesity is estimated to reach 49% by 2030. In the US, obesity-related chronic disease has a medical burden of $1.71 trillion.
GLP-1 receptor agonist, Semaglutide, has been approved for weight loss. However, half of the patients do not respond to it. There is an urgent need for other effective treatments for obesity.

PRODUCT: A novel therapy that genetically changes white adipocytes into brown adipose tissue (BAT)-like tissue to increase energy expenditure, glucose tolerance, and insulin sensitivity.

COMPETITIVE ADVANTAGE/DIFFERENTIATION:

- Removing and grafting fat are commonly used clinical procedures in humans.
- More brown fat can also help prevent cancer and aging.

DATA: Direct AAV-CRISPRa upregulation of brown fat genes in white fat reduces weight gain and improves glucose and insulin sensitivity in mice on high fat diet and genetic obesity mouse models.

Transplantation of engineered white fat that is turned into ‘brown’ fat reduces weight gain and improves glucose and insulin sensitivity in mice on high fat diet and genetic obesity mouse models.

Targeting Mucus Plugs to Improve Lung Health

John Fahy, MD, MS
Co-founder, Aer Therapeutics
UCSF Pulmonologist and Innovator

PROBLEM:

- Between 30% and 50% of COPD patients with severe and very severe COPD suffer from airway obstruction caused by mucus plugs.
- Mucus plugs reduce lung function and diminish quality of life.
- There are no drugs approved to effectively liquify mucus plugs (mucolytics) in patients with COPD.

SOLUTION:

- Fexlamose is a novel inhaled best-in-class therapeutic candidate designed to improve lung health by liquifying mucus plugs.
- Fexlamose is a thiol-modified carbohydrate ("thiol-saccharide") which cleaves mucine disulfide bridges to liquefy ("lyse") mucus plugs.

FUNDING:

- >$18M in NIH funding; $36M Series A (Canaan, Orbimed, Hatteras)

PROGRESS

- Phase 1 studies in healthy volunteers completed
- Phase 2 POC started in q4 2024
- Top line efficacy data expected in q1 2026

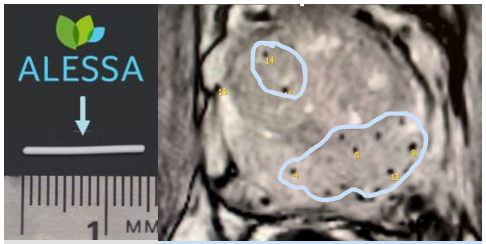
LEARN MORE:

ALESSA THERAPEUTICS

We drive innovation in oncology and solid organ diseases through development of organ selective therapy for early interception and treatment of the prostate disease

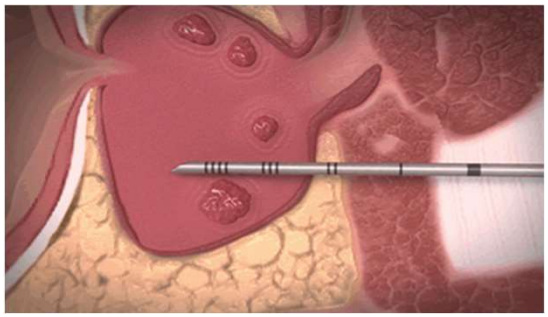
UCSF

Pamela Munster, MD
Founder and CSO,
Alessa Therapeutics
UCSF Professor of Medicine and Innovator



Pre-implant seed

Post-implantation seeds in cancerous human prostate



PROBLEM:

- 1 in 6 men will be afflicted with prostate cancer during their lifetimes, 30k will die every year.
- 12M men in the US seek treatment for benign prostate hyperplasia every year.
- Current therapies mainly centered around systemic testosterone ablation.

SOLUTION:

- Implant and delivery systems for localized, sustained drug delivery without systemic side effects.
- Focused on treatment of localized prostate cancer and BPH.
- Robust pipeline of target specific organ selective strategies.

TRACTION:

- $15M in seed funding led by Mission BioCapital joined by Johnson & Johnson
- Ongoing clinical trial with Enolen

LEARN MORE:

CHROMA MEDICINE

Reimagining Genome Regulation

UCSF

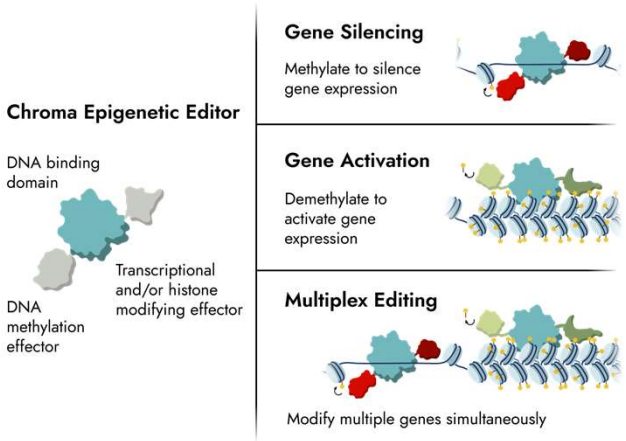
Luke Gilbert, PhD
Co-founder, Chroma Medicine
UCSF Professor and Innovator

PROBLEM:

- To build single dose therapeutics that durably control expression of human genes.

SOLUTION:

- Single-dose genomic medicines that harness epigenetics for durable and heritable gene silencing.
- A modular platform for epigenetic editing to address a wide range of complex diseases.



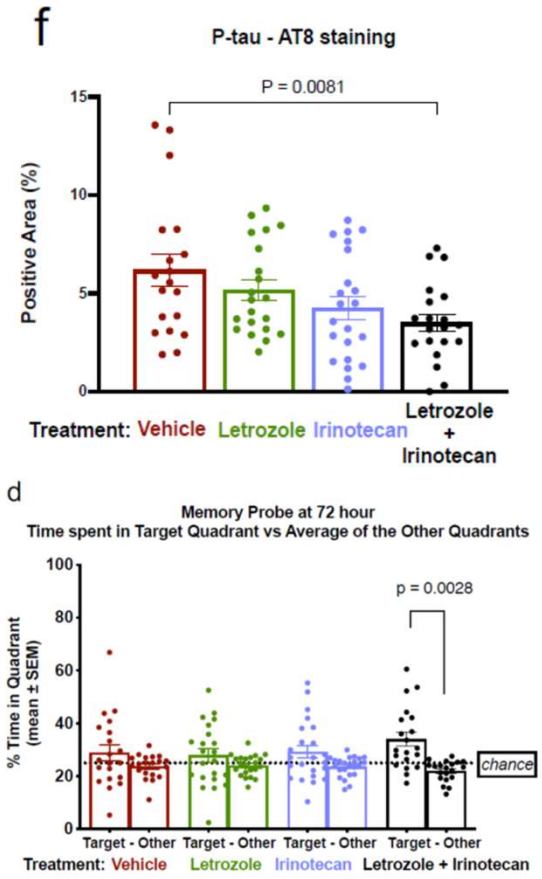
TRACTION:

- Chroma Medicine and Nvelop Therapeutics **UNITE** to Form **nChroma Bio,** Securing $75 Million to Accelerate Genetic Medicines
- Chroma Medicine Demonstrates Robust and Durable HBV Silencing with CRMA-1001
- >$250M in Funding

LEARN MORE:

Combo therapy (letrozole + irinotecan) for Alzheimer's Disease

Marina Sirota, PhD
Assistant Professor
Bakar Computational Health Sciences Institute, UCSF



DISEASE/INDICATION: Alzheimer's Disease

UNMET NEED:

- Current treatments have **limited efficacy and only delay disease progression** due to disease heterogeneity

PRODUCT: Combination of letrozole and irinotecan treating AD

- Letrozole is an off-patent chemotherapy for breast cancer
- Irinotecan is an off-patent chemotherapy for colorectal cancer

COMPETITIVE ADVANTAGE/DIFFERENTIATION:

- Improvement vs. existing AD treatment with the potential to reverse disease progression

DATA:

- Validation of drug candidates using real world evidence from UC-wide EMR database, showing reduced risk of AD
- In vivo validation study in AD mouse model shows combination can rescue:
  - Short-term, long-term, and spatial memory
  - AD pathologies, e.g., hippocampal volume, Beta-amyloid pathology, P-tau pathology

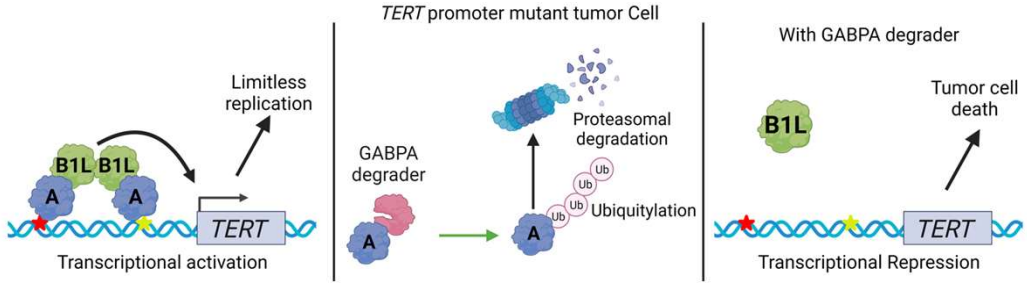
Targeting Tumor Immortality by Degrading the Cancer-Specific Regulator of TERT Expression

Joseph F. Costello, PhD
Co-founder, Curaidh Bio
UCSF Professor and Karen Osney Brownstein Endowed Chair in Molecular Neuro-Oncology

Noriyuki Kasahara, MD, PhD
Co-founder, Curaidh Bio
UCSF Professor and Endowed Chair Neurological Surgery and Radiation Oncology

PROBLEM:

- Mutation in the TERT promoter enables unlimited cell proliferation for over 50 cancer types, including glioblastoma.
- The SOC for glioblastoma has remained unchanged for decades and the average survival rate is 15 months.



SOLUTION:

- GABP degrader reduces TERT expression in tumor cells harboring the TERT promoter mutation.
- Reduced TERT causes a shortening of telomeres in cancer cells and improves survival in an orthotopic xenograft mouse model of GBM.
- Replicating retroviral delivery system only infects dividing cells and will be used for cancer specific delivery of the degrader.

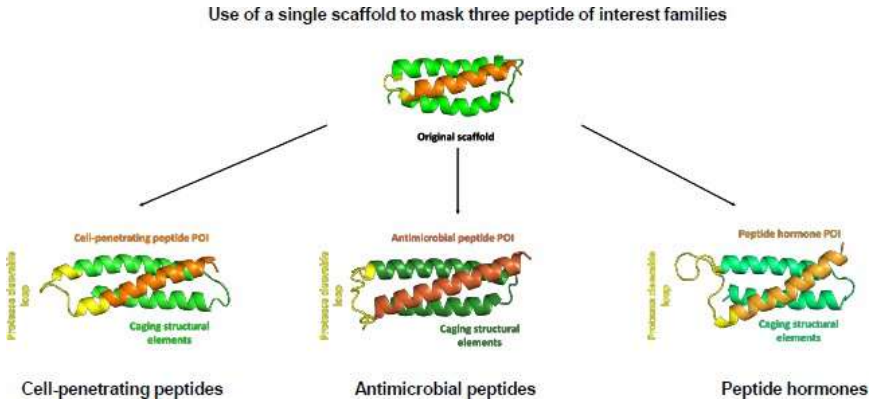
TRACTION:

- Provisional patent filed. Publication under revision at Nature Genetics.

LEARN MORE:

De-Novo Designed Peptide Delivery System

Bill Degrado, PhD
Professor, Pharmaceutical Chemistry
UCSF Innovator



INDICATIONS: Anti-infectives, Theranostic Radio-Therapies for Oncology, Thrombus Imaging agents

UNMET NEED: Current technologies utilizing targeted delivery systems don't have the specificity needed to provide to provide the desired efficacy of treatment and avoidance of drug related side effects.

PRODUCT: De-novo designed peptide delivery system that masks bio- active domains of protein cargos and enables delivery to extracellular and intracellular targets, and delivery of anti-microbial peptides or peptide hormones with high levels of specificity.

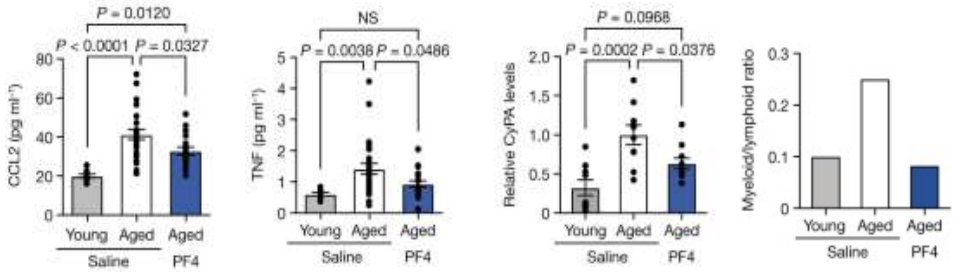
COMPETITIVE ADVANTAGE / DIFFERENTIATION:
High level ofspecificity in delivery, flexibility in range of cargos that are able to be delivered.

DEVELOPMENT STAGE: Pre-clinical

Development of Platelet-Derived Exercise Mimetics as a Treatment for Alzheimer's Disease and Related Dementias

Saul Villeda, PhD
Co-founder, Ceiba Bio
UCSF Associate Professor, Anatomy

Recombinant Pf4 (i.v.) every 3 days (q3day) in aged mice (> 17 mo) reverses age associated inflammation (CCL2, TNF, CyPA) and lowers myeloid to lymphoid ratio



DISEASE/INDICATION: Alzheimers Disease (AD) and related dementias are progressive neurodegenerative diseases where the current standard of care is to address symptoms and not the underlying cause.

UNMET NEED: Current therapies are symptom-modifying only, have no effect on disease progression. New therapeutics are needed to address both AD symptoms and progression.

PRODUCT: Biologics that ameliorate disease. These can be administered peripherally and still have an effect disease.

COMPETITIVE ADVANTAGE/DIFFERENTIATION:

- Potential for dual approach (symptom management + neuroprotection)

DATA: This research has been published in *Nature* and *Science.* A novel composition of matter was generated for PF4 and an optimized screening assay is in place for GPLD1

Novel Target Platform for Metabolic Inflammation, Fibrosis and Inflammasome Pathologies

Adam Renslo, PhD
Co-founder, Elgia Therapeutics
UCSF Professor and Associate Dean for Entrepreneurship

Michelle Arkin, PhD
Co-founder, Elgia Therapeutics
UCSF Professor and Chair of Pharmaceutical Chemistry

PROBLEM:

- Dramatic rise in the incident of chronic inflammatory diseases presents a global health burden.

SOLUTION:

- Elgia Therapeutics targets caspase-1 for hidradenitis suppurativa as initial indication.
- Our novel, targeted covalent inhibitors disrupt key cellular processes involved in metabolic, inflammatory, and fibrotic diseases.

TRACTION:

- ~$5M in seed funding to date.

LEARN MORE:

ENCELLIN

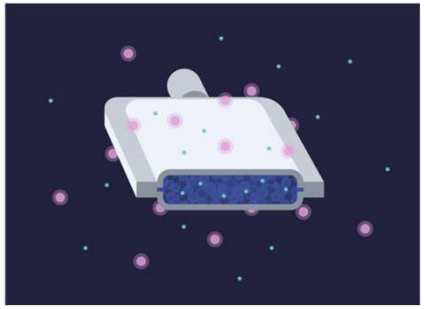
Advancing next generation therapies, starting with endocrine disorders.

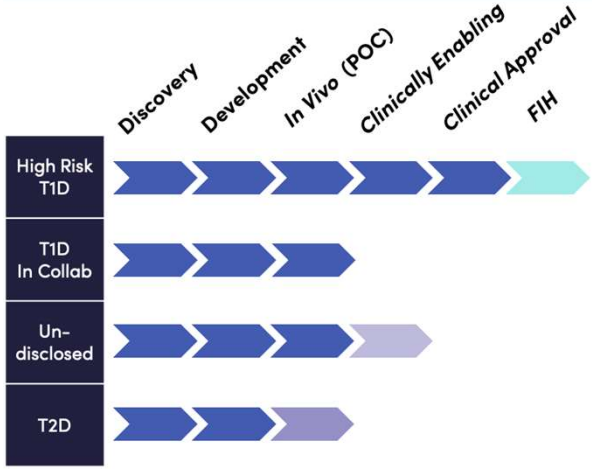
UCSF

Crystal Nyitray, PhD
CEO, Encellin Founder
Founder, Inventor
UCSF, Sanofi, YCombinator

PROBLEM:

- Next generation therapies to help patients with chronic unmet clinical needs.
- Starting with endocrine disorders.





SOLUTION:

- Encapsulated Cell Replacement Therapy (ENCRT).
- Encellin's ENCRT allows enclosed cells to function like smart molecular factories, releasing therapeutics when needed.

TRACTION:

- ~$10M in funding 2023
- Active and enrolling clinical trial

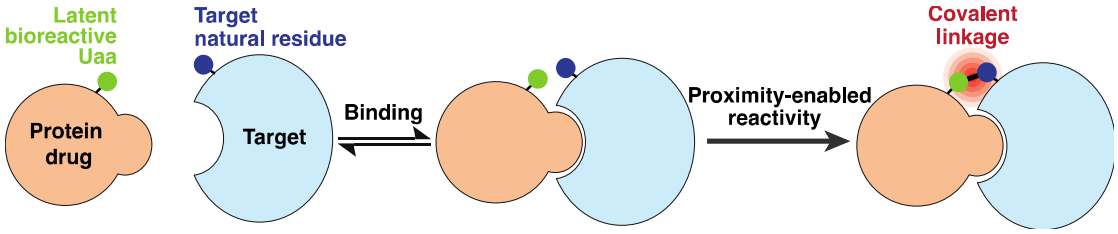
LEARN MORE:

Enlaza Therapeutics

Pioneering Covalent Biologics

UCSF

Lei Wang, PhD
Inventor, Enlaza Therapeutics
UCSF Professor and Innovator



PROBLEM:

- Proteins bind target reversibly.
- Most therapeutics still suffer from low tumor retention and high off-target toxicity.

SOLUTION:

- New generation of covalent 'War-Lock™' biologics
- Proprietary unnatural amino acids.
- Protein drugs derived from the platform can be modified to incorporate various payloads, creating antibody-drug conjugates (ADCs) or radioligand therapies (RLTs) with specific target tissue delivery, without the need for half-life extension engineering.[1]

TRACTION:

- $100M in Series A lead by Life Sciences Group of J.P. Morgan Private Capital

LEARN MORE:

ePhective Therapeutics: bacteriophage enabled in-situ therapeutic protein production

Joe Bondy-Denomy PhD
Co-founder, 153 Therapeutics
UCSF Associate Professor,
Microbiology and Immunology

Category	Competition	Kill Bacteria	Self Amplify	Broad Spectrum	Increased Killing	Protein Production	Early Focus on DLP
Phages engineered for broad killing & therapeutic protein production	ePhective	✓	✓	✓	✓	✓	✓
Products derived from phage	Lysando, Micreos	✓	X	✓	X	X	X
Natural unmodified phage	Phagelux, Intralytix	✓	✓	X	X	X	X
Non replicating easily engineered model phage	Snipr, Eligo	✓	X	X	X	X	X
Replicative easily engineered model phage	Phico, BiomX, Locus, Armata	✓	✓	✓	X	X	X

DISEASE/INDICATION: ePhective's initial indication will be acute pseudomonas aeruginosa Hospital/Ventilator Acquired Pneumonia (HAP/VAP)

UNMET NEED: HAP/VAP is the leading cause of hospital-acquired infections resistant to all existing drugs

PRODUCT: Engineered phage that can produce antimicrobial peptides in-situ

COMPETITIVE ADVANTAGE/DIFFERENTIATION:

- ePhective's technology will combine the benefits phage-mediated and antimicrobial peptide-mediated bacterial killing to reach more bacteria

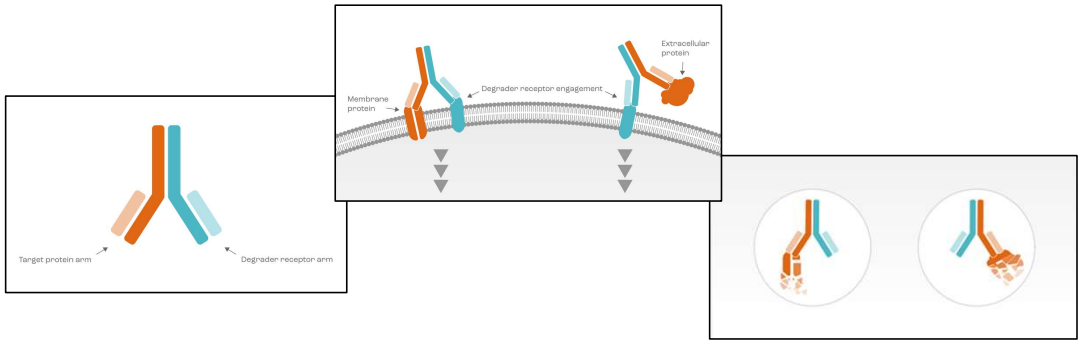
DATA: in progress

Expanding Protein Degradation to Membrane and Extracellular Targets

Jim Wells, PhD
Co-Founder, EpiBiologics
Founding Director, Small Molecule Discovery Center (SMDC)
Director, Antibiome Center
UCSF Innovator

PROBLEM:

- First generation protein degradation approaches target intracellular proteins only.
- 40% of the proteome is unaccounted for.
- Better targeted therapies are still needed.
- Need modalities that can avoid complex manufacturing and short half-life and localize degradation to disease tissue.



SOLUTION:

- EpiTAC platform leverages bispecific antibodies and a novel atlas of tissue-selective degrader receptors to drive strong efficacy
- Bispecific antibodies are scalable, manufacturable, and have good pharmacological properties that enable long half-life and durable responses.

TRACTION:

- Demonstrated POC for soluble and membrane targets, including GPCRs
- Raised >$70M in Series A, initiating Series B to move into the clinic

LEARN MORE:

Redefining Drug Discovery for Rare Genetic Epilepsies

Scott C. Baraban, PhD
Co-founder, Epygenix Therapeutics
Professor, William K. Bowes Jr. Endowed Chair in Neuroscience Research
UCSF Innovator

PROBLEM

- 30-40% of epilepsy is caused by genetic mutation.
- Most genetic epilepsies are pharmaco-resistant, emerge early in life & are life-threatening.
- Existing antiepileptic medications were not identified using genetic epilepsy models.

SOLUTION

- 'Aquarium-to-Bedside' drug discovery using genetically modified zebrafish models in high-throughput phenotype-based drug screening.

TRACTION

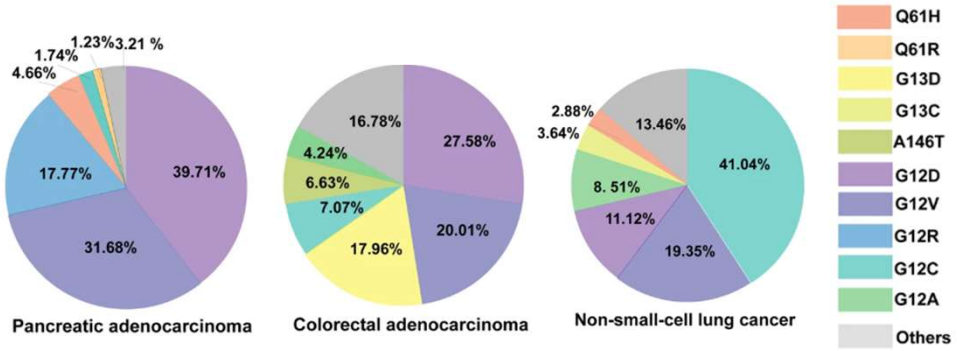
- Epygenix Therapeutics, Inc **ACQUIRED** by Harmony Biosciences in April 2024
- >$35M in seed funding
- Six drug candidates licensed from UCSF w/ method-of-use and formulation IP

LEARN MORE:

Kras Targeting Small Molecules

Kevan Shokat, PhD
UCSF Professor, Pharmaceutical Chemistry

Ziyang Zhang, PhD
UCB Professor, Chemistry and Chemical Biology



DISEASE/INDICATION: Kras is considered to be the most common oncogenic gene driver in human cancers.

UNMET NEED: Despite it's role as a driver oncogene, Kras was considered undruggable until the Shokat Lab identified the switch II binding pocket, enabling the development of small molecules that target the mutant KRasG12C cysteine. This work has continued enabling the development of more small molecules targeting various Kras mutants.

PRODUCT: Small molecules that each individually target KrasG12D, G12S, G12R and G13C.

COMPETITIVE ADVANTAGE/DIFFERENTIATION: Existing, marketed small molecules target KRasG12C which is the most common mutation in NSCLC. KRasG12D and other mutation are more common in other cancer types.

DATA: this research has been published in *Nature, Journal of the American Chemical Society* and *eLIFE*

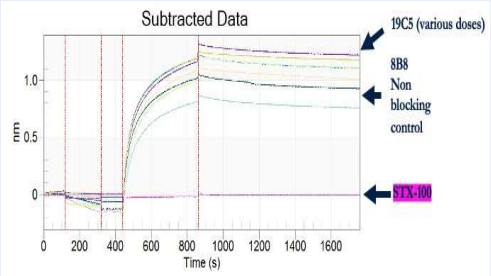
Lasso Therapeutics

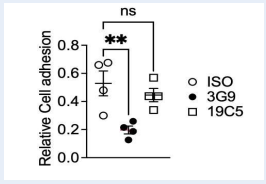
Precision Allosteric Antibody Therapeutics

Steve Nishimura, MD
Co-founder, Lasso Therapeutics
Chief of Pathology; Endowed Chair and Professor at UCSF

Yifan Cheng, PhD
Co-founder, Lasso Therapeutics UCSF Professor, Biochemistry and Biophysics; HHMI investigator

19C5 lead does not block binding





DISEASE/INDICATION: IPF, additional fibrosis indications driven by TGFβ pathway, cancer and autoimmune

UNMET NEED: Idiopathic Pulmonary Fibrosis is a disease with a median survival of 2–5 years. There are currently no therapeutics that reverse progression or improve survival, and current therapies demonstrate significant AE. Lung transplant is the only effective therapy and new drugs are sorely needed.

PRODUCT:

- Platform for discovery and development of novel allosteric mAbs
  - Proprietary structural pipeline applicable in multiple therapeutic indications
  - A new class of allosteric antibody specifically designed to modify the magnitude and direction of cell:cell signaling
  - Safer targeting of cell:cell signaling

COMPETITIVE ADVANTAGE/DIFFERENTIATION:

- Novel allosteric mAbs with superior precision, efficacy and safety
- Competitive programs terminated for lack of safety, efficacy regardless of modality

DATA/PROGRESS TO DATE:

- Lasso allosteric antibodies inhibit receptor signaling without blocking binding resulting in less off-target activation compared to competitive programs: lead program to αvβ6
- Preliminary in vivo data support safety and efficacy of lead

MAITRX

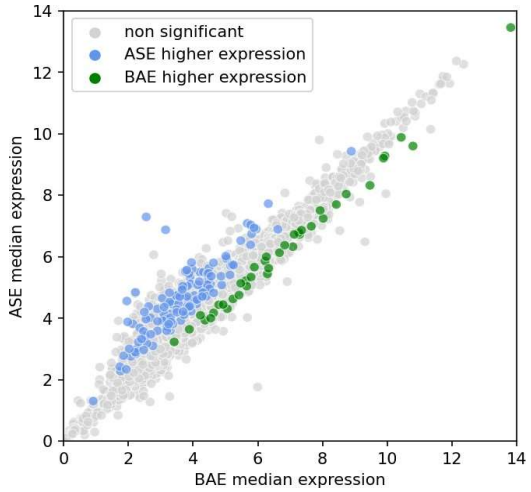
Allelic-informed target and drug discovery

UCSF

Franklin Huang, MD, PhD

Associate Professor,
Medicine and Urology

Expert in genomics and practicing physician caring for patients with prostate cancer



DISEASE/INDICATION: Various cancers, prostate cancer being the initial focus and autoimmune diseases

UNMET NEED: Existing mutational discovery platforms focus on activating mutations. Many disease-causing genetic abnormalities, for example TERT promotor mutations, cause dysregulation and allele-specific expression is a marker of such dysregulation.

PRODUCT: *In silico* assay to screen and interrogate patient samples to identify allelically imbalanced genes when known genetic markers cannot be found. Machine-learning algorithms that incorporate clinical, genomic, and experimental data to identify allele-specific markers of unusual response, are used to predict drug response, and regulatory pathways that can be targeted

COMPETITIVE ADVANTAGE/DIFFERENTIATION:

- Integrates various inputs
- Uses AI to train platform
- Not limited to liquid biopsies
- Can discover novel pathways

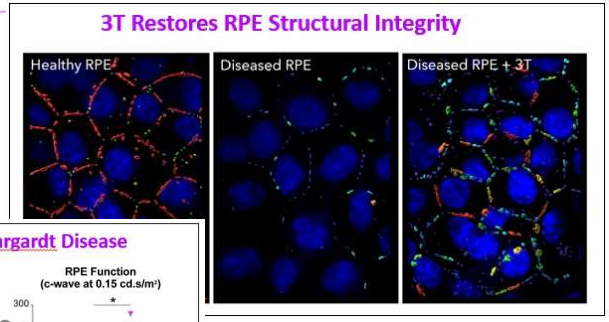
DATA: The screen has identified allele-specific events found in metastatic castration resistant prostate cancer not found in less aggressive prostate cancer

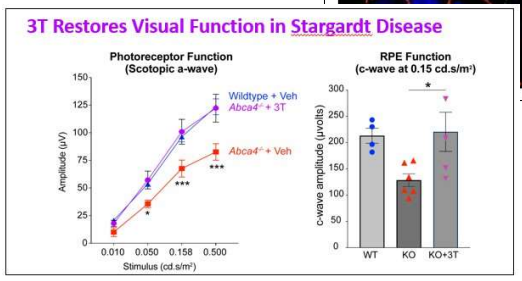
Multimodal Therapeutic for Dry-AMD and Stargardt

Aparna Lakkaraju, PhD
Professor, Ophthalmology
UCSF Innovator

MOA:

Pre-clinical Results:





DISEASE INDICATION: Dry AMD or geographic atrophy causes progressive irreversible vision loss in ~ 50 million people worldwide.

UNMET NEED: Recently approved treatments for dry AMD do not delay the progression of vision loss. There are no approved therapies for Stargardt disease, which is the most common cause inherited macular degeneration.

PRODUCT: Small molecule drug that targets multiple pathogenic nodes implicated in macular degenerations (RPE injury, complement activation, drusen deposition, metabolic stress, etc.)

COMPETITIVE ADVANTAGE / DIFFERENTIATION:
3T is the first novel small molecule drug that demonstrates restoration of visual function in preclinical models.
Strong safety and retinal bioavailability profile make 3T an outstanding candidate for chronic diseases like dry AMD and Stargardt disease.

DEVELOPMENT STAGE: Currently running IND enabling studies, and is raising $5M in seed funding to run FIH clinical trials. ~$10M non- dilutive funding has been invested up to this point.

New generation bitopic BCR-ABL inhibitors

Kevan Shokat, PhD
UCSF Professor,
Cellular, Molecular
Pharmacology

DISEASE/INDICATION: Chronic Myeloid Leukemia

UNMET NEED: Scientists at UCSF have developed a novel class of BCR-ABL inhibitors that engages two binding sites in BCR-ABL simultaneously. This two-site binding (bitopic) mechanism of action is unprecedented against BCR-ABL, one of the most well-validated targets in oncology.

PRODUCT: Bitopic BCR-ABL Inhibitors

COMPETITIVE ADVANTAGE/DIFFERENTIATION:

- Increased potency (especially against resistance mutations such as the T315I mutant in CML)
- Higher target specificity due to avidity (active site AND allosteric site recognition needed for binding)
- Potentially reduced cardio-toxicity
- Deeper target inhibition at BCR-ABL, potentially increasing the proportion of patients experiencing cure

DATA: POC data supporting leads

Next-gen vaccine for Neisseria infections

Peter Beernink, PhD
Professor, Pediatrics
School of Medicine

DISEASE/INDICATION: Infections caused by Neisseria bacteria e.g., meningitis and gonorrhea

UNMET NEED:

Gonorrhea

- Infection by N. gonorrhoeae is the second most common STI with significant direct medical costs in the US ($271M) and globally
- Recent emergence of antibiotic-resistant gonorrhea further highlights the need for a vaccine
- No approved vaccine for gonorrhea; GSK's gonorrhea vaccine was granted FDA fast-track designation in 2023, currently in Phase I/II

Meningitis

- Existing Men B vaccines has limited efficacy against certain Men B strains due to heterogenous expression of factor H binding protein (fHBP), a key component of Men B vaccines

PRODUCT: Next-gen vaccine for Neisseria infections with increased immunogenicity

- NspA (Neisserial Surface Protein A) is a highly conserved Neisseria antigen, similar to fHBP
- NspA mutants with decreased binding to factor H increases vaccine immunogenicity

COMPETITIVE ADVANTAGE/DIFFERENTIATION:

- Improved protection against Neisseria infections vs. existing vaccines with only fHBP

DATA:

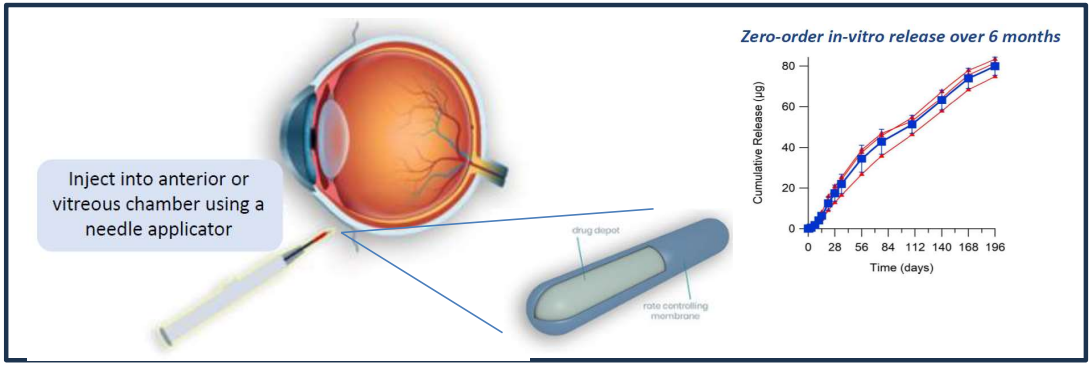
- Identified mutants of NspA with decreased factor H binding, measured by ELISA and surface plasmon resonance (SPR)
- Additional animal studies ongoing

Oculinea

Novel Delivery of Ocular Therapeutics

UCSF

Robert Bhisitkul, MD, PhD
Co-founder, Oculinea Inc
UCSF Professor of Ophthalmology and Innovator



PROBLEM:

- Adherence with medications is a fundamental problem in the care of glaucoma patients as 24–59% fail to receive the intended treatment.
- Non-adherence to therapy leads to irreversible loss of vision.

SOLUTION:

- Long acting zero-order drug delivery of small molecules & biologics for 6-months or longer. Office based procedure: **M**iniaturized **I**njectable **D**elivery **S**ystem (**MIDS**).
- Transform treatment for glaucoma & retinal diseases with better clinical outcomes through patient compliance.

TRACTION:

- Lead Program: Glaucoma MIDS at IND Enabling Stage
- Accelerated regulatory pathway: FDA's 505(b)(2)
- 12 Issued Patents (Domestic and International)
- Partnerships with major pharmaceutical companies

LEARN MORE:

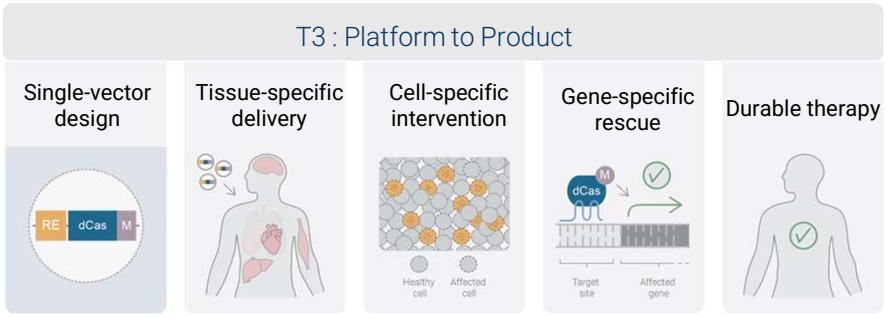
Targeted Gene Therapy to Transform the Lives of People Living with Severe Genetic Diseases

Navneet Matharu, Ph.D.
Co-founder/CSO, Regel Tx
UCSF Assistant (Adjunct) Professor
IGI-WIES fellow

Nadav Ahituv, Ph.D.
Co-founder Regel Tx
UCSF Professor, Bioengineering
Director, Institute for Human Genetics

PROBLEM:

- Disease modifying therapies for haploinsufficient disorders are lacking.
- Approx 600 such disorders have high unmet need.
- Targeted genetic therapies are needed.



SOLUTION:

- Clinical vector with a dCas module and an engineered enhancer.
- Targeted delivery with a one-time injection in the affected system.
- Restricts the intervention to the affected cells
- The dCas module normalizes the level of gene expression.

TRACTION:

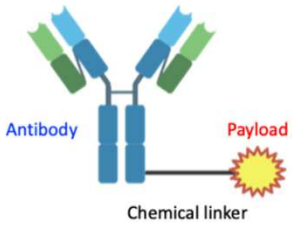
- Raised $6M seed + BD partnership
- 3 programs under a Research Collaboration and Option Agreement with Sarepta Therapeutics

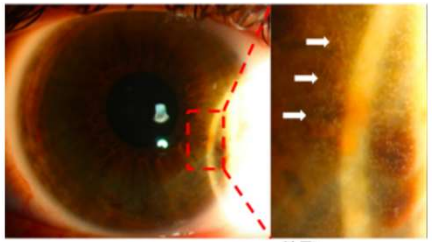
LEARN MORE:

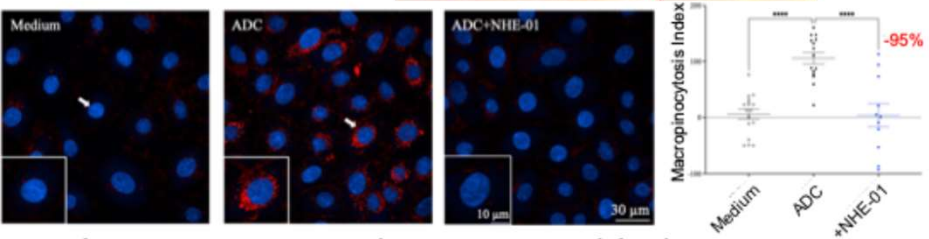
Repurposed Eye Drop for Antibody-Drug Conjugate (ADC) Corneal Toxicity

Neel Pasricha, MD
UCSF Assistant Professor, Ophthalmology

Onur Cil, MD, PhD
UCSF Associate Professor, Pediatric Nephrology







DISEASE/INDICATION: ADC corneal toxicity

UNMET NEED: ADC corneal toxicity is a leading adverse event in ADC therapy, occurring with 50% of all ADCs. This affects >50,000 US patients annually and leads to ADC dose interruptions, including 50% dose delays, 25% dose reductions, and 5% discontinuations. Current therapies have limited efficacy.

PRODUCT: Topical NHE-01 eye drop reduces macropinocytosis and ADC internalization, which is the main off-target toxicity mechanism.

DATA: NHE-01 reduces macropinocytosis by 95% and ADC internalization by 40% in human corneal epithelial cell culture. Pursuing preclinical rabbit model testing (AbbVie) and first-in-human proof-of-concept testing in humans (JNJ). If successful, plan for 505(b)(2), orphan drug, priority review, and breakthrough therapy designations.

Unique Platform to go from Sequence to Systems to Drugs

UCSF Co-founders

Nevan Krogan, PhD
UCSF Professor

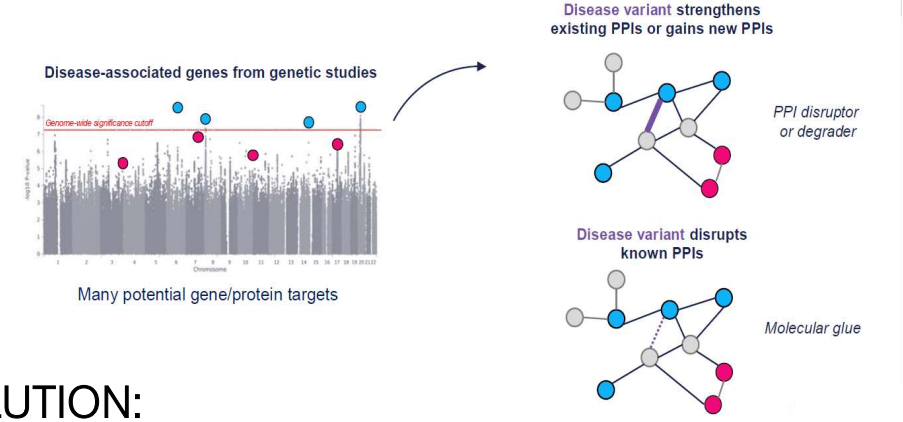
Sourav Bandyopadhyah, PhD
UCSF Professor

Natalia Jura, PhD
UCSF Professor

Kevan Shokat, PhD
UCSF Professor

PROBLEM:

- Drug discovery and development is LONG (10-15yrs), COSTLY ($1-2 billion) and HIGH-RISK with a 90% clinical failure rate due to the lack of clinical efficacy, unmanageable toxicity, and poor drug-like properties



SOLUTION:

- Combining multimodal data from several advanced technologies: from disease associated genes to causative protein networks
- Identifying convergent biological pathways driven by disease causing proteins
- Discovering new high-confidence actionable therapeutic targets and integrating AI for novel therapeutic discovery

TRACTION:

- $78M Series A funded in 2022

LEARN MORE:

Uncovering the Invisible Cancer Surfaceome

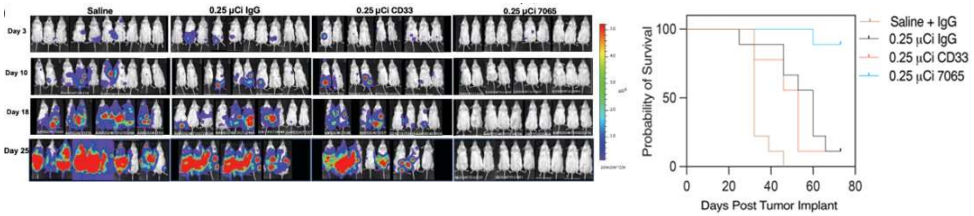
Arun Wiita, MD, PhD
Scientific Co-Founder
Proteomics, blood cancers, preclinical development, and clinical translation of novel immunotherapies

Rob Flavell, MD, PhD
Scientific Co-Founder
Development and clinical translation of novel radio-immunotherapies

Hector Huang, PhD
Head of Proteomics
Deep expertise in MS-based proteomics and discovery of cancer-specific proteoforms

Althea Stillman, PhD
Advisor
XiR, UCSF Experienced life science investor and company builder

ST-001 has better efficacy and survival compared to clinical stage Lintuzumab (anti-CD33)



DISEASE/INDICATION: Acute Myeloid Leukemia (AML) and solid tumors

UNMET NEED: There is a lack of immunotherapy targets that are highly cancer-specific (i.e. not also expressed on normal tissues) resulting in significant toxicity and disappointing clinical efficacy.

PRODUCT: Proteomic platform for novel immunotherapeutic target discovery in AML and solid tumors, based on tumor-specific proteoform identification

- Best-in-Class Radioimmunotherapeutic for treatment of AML
  - active Integrinβ2-specific antibody+proprietary linker and chelator technology
- Discovery program in colorectal and prostate cancers ongoing

COMPETITIVE ADVANTAGE/DIFFERENTIATION :

- SEEN Platform improves immunotherapy targeting by identifying cancer-specific protein features (surface protein conformations, abnormal surface trafficking, post-translational modifications) invisible to other discovery methods such as RNA-seq

DATA: Anti-active Integrinβ2 CAR-T cytotoxicity is highly specific for AML while not toxic to normal hematopoieitic cells, both in vitro and in vivo, unlike other leading AML CAR-T targets (*Nature Cancer,* 2023)
doi: https://doi.org/10.1101/2022.10.10.511511

Developed novel proteomics-based methodology in solid tumor patient samples

Siolta Therapeutics

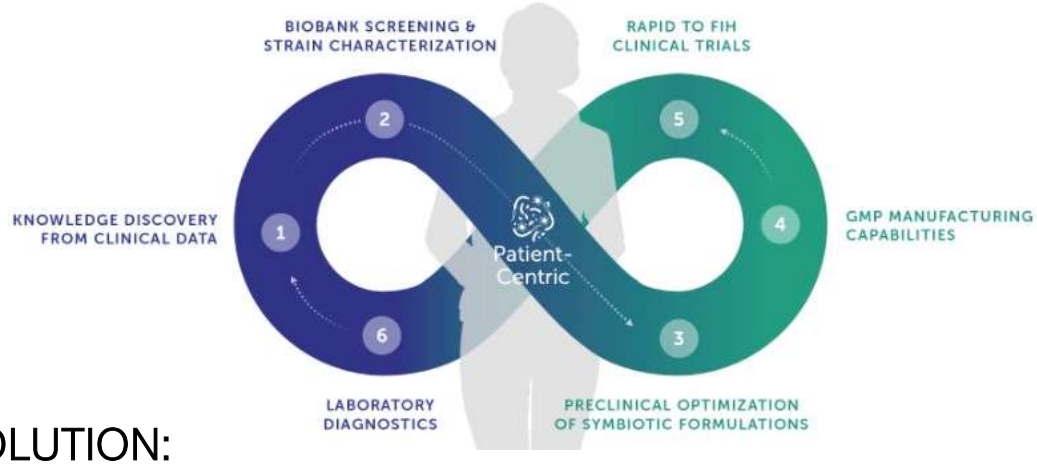
Developing Live Biotherapeutics Targeting Core Drivers of Disease

UCSF

Nikole Kimes, PhD
Co-founder and CEO,
Siolta Therapeutics
UCSF Inventor & PhD
Postdoc Alum

PROBLEM:

- Addressing the underlying cause of IgE-mediated diseases, including atopic dermatitis, food allergy, allergic asthma and allergic rhinitis
- Developing live biotherapeutics that target the core drivers of disease through immunomodulation.



SOLUTION:

- Patient-centric platform.
- Microbiome data analysis, machine learning, anaerobic microbiology.
- Optimizes multi-strain live biotherapeutics to prevent/treat disease.

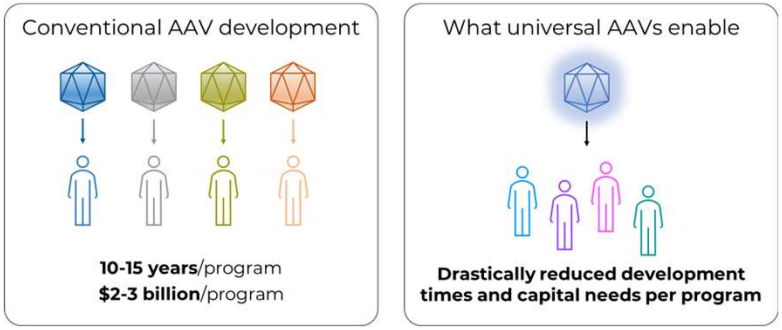
TRACTION:

- $12M Series C for clinical development co-led by SymBiosis and Khosla Ventures
- $50M in funding

LEARN MORE:

Universal AAV Immuno-Gene Therapy for Cancer

Nicole K. Paulk, PhD
CEO, Founder, President
Siren Biotechnology
Prior UCSF Professor



PROBLEM:

- No effective therapies for brain cancers

TRACTION:

- Announced partnership with Catalent for AAV gene therapy manufacturing for cancer
- Awarded $4M in grant funding from California Institute for Regenerative Medicine (CIRM)
- Awarded ODD and RPD FDA designations

SOLUTION:

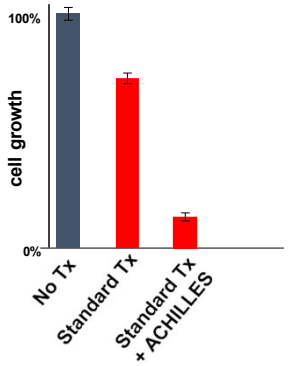
- Combining AAV gene therapy and cytokine immunotherapy into a single, reimagined modality overcomes key challenges in destroying tumor cells and eliciting anti-tumor immunity.
- 1st AAV drug product that can treat more than one disease.
- A universal gene therapy reduces clinical development times, manufacturing timelines, and capital needs per program.
- Countless solid tumor cancer patients will be eligible regardless of tumor type or mutations with this breakthrough approach.

LEARN MORE:

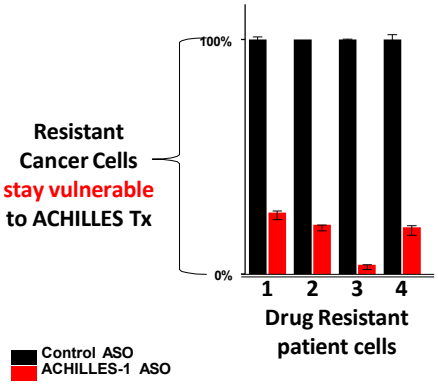
Spartia Therapeutics

Targeting oncogenic RNAs for the treatment of cancer

Susana Ortiz-Urda, MD/PhD MBA
UCSF Associate Professor, Dermatology



ACHILLES-ASOs work together with standard melanoma treatments for increased efficacy in mouse models



Cancer cells retain sensitivity to repeated ACHILLES-ASO treatment to avoid resistance mechanisms

DISEASE/INDICATION: Oncology, melanoma is the lead indication

UNMET NEED: More than 50% of cancer patients do not respond to either immune or targeted therapies due to initial or acquired treatment resistance

PRODUCT: RNA discovery platform to identify and target oncogenic RNAs; a portfolio of novel anti-cancer ASOs for MAPK cancers

COMPETITIVE ADVANTAGE/DIFFERENTIATION:

- Eliminating oncogenic RNAs specifically and potently kills tumor cells, unlocking a novel class of cancer-selective therapeutics
- Oncogenic coding/non-coding RNAs are a drug target class that may overcome resistance and toxicity seen in current MAPK drugs

DATA: Preclinical data demonstrating mechanism, efficacy, and preliminary safety in cell line and rodent models

Exploiting Ferro-Addiction in Tumors with Proprietary Ferrous Iron REactive (FIRE) Linker Technology

tatara therapeutics

UCSF

UCSF Co-founders

Adam Renslo, PhD
Tatara Therapeutics
UCSF Professor and Associate Dean for Entrepreneurship

Eric Collisson, MD
Tatara Therapeutics
Oncologist and Professor Fred Hutchinson Cancer Center (Formerly UCSF)

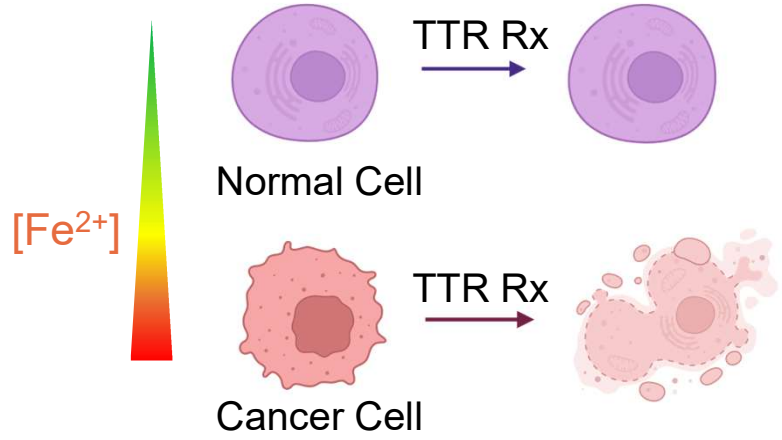
PROBLEM:

- Cancer therapeutics act systemically, with systemic toxicities that reduce therapeutic index and limit efficacy.

SOLUTION:

Tumor-conditional activation of linkers for prodrug and ADC modalities

- Ferrous Iron REactive (FIRE) linker technology



- Broad scope of utility across multiple Tx modalities
- Current focus on topoisomerase-I payload delivery

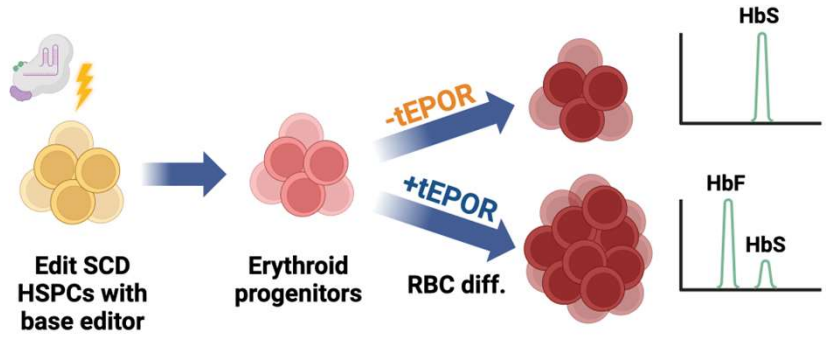
TRACTION:

- ~$6M in VC and home office investment to date
- Multiple patent families: US 11,014,955; 11,072,594; WO 2023/049829

LEARN MORE:

tEPOR: Next Generation RBCs for Hemoglobinopathy Treatment

Kyle Cromer, PhD
UCSF Innovator and
Assistant Professor
Dept. of Surgery & Dept. of
Bioengineering &
Therapeutic Sciences



PROBLEM:

- 20% of sickle cell disease patients have a matched donor, yet <1% of patients in U.S. receive a bone marrow transplant indicating a major unmet medical need.
- *Ex vivo* CRISPR-mediated editing allows every to patient to have a “donor”, however myeloablation-associated mortality is a major barrier to safe correction of disease.
- *In vivo* editing has low delivery & editing frequencies.

SOLUTION:

- Genome editing is used to introduce a naturally occurring truncated erythropoietin receptor (tEPOR).
- By increasing production of functional RBCs, this editing strategy *may compensate for low in vivo editing frequencies* in HSCs.
- This editing strategy *may eliminate the need for myeloablation.*

TRACTION:

- Multiple patent disclosures filed to protect IP
- Work awarded American Society of Hematology Junior Faculty Scholar Award

LEARN MORE:

TheraPaint
Molecular Painting of Disease

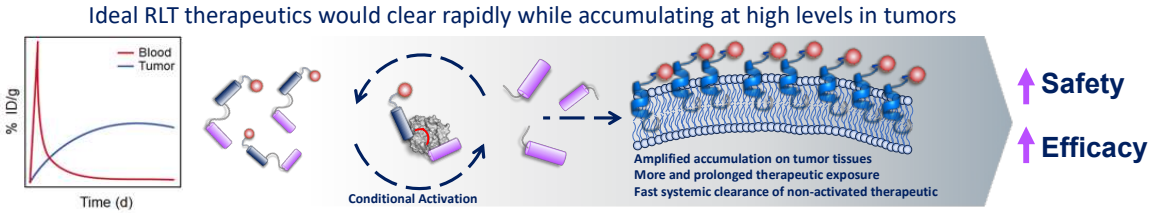
Re-imagining radioligand therapy with tumor conditional membrane binding probes

UCSF

Michael J Evans, PhD
UCSF Professor

Charles S. Craik, PhD
UCSF Professor

Lawrence Fong, MD
UCSF Professor

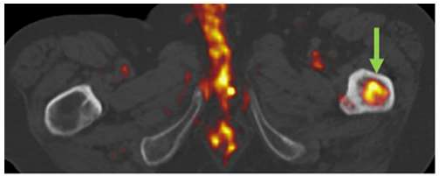


PROBLEM:

- **Tumor responses to radioligand therapy (RLT) are often transient** and/or variable among patients.
- **New drug delivery strategies to expand the therapeutic window** for RLT are needed.

SOLUTION:

- **Restricted interaction peptides (RIPs)** are small peptides that use a two step targeting strategy to improve tumor delivery and retention of isotopes
- Recent clinical data with a Cu-64 labeled RIP (NCT05888532) establish the safety and tumor detection



TRACTION:

- First in human imaging data with a therapeutic DC planned at UCSF in Q2 2025
- Broad IP portfolio filed

LEARN MORE:

Tiller Therapeutics

Small Molecule Drug Conjugates for Prostate Cancer

Alan Ashworth, PhD, FRS
President, UCSF Cancer Center
BRCA2/PARP inhibitors

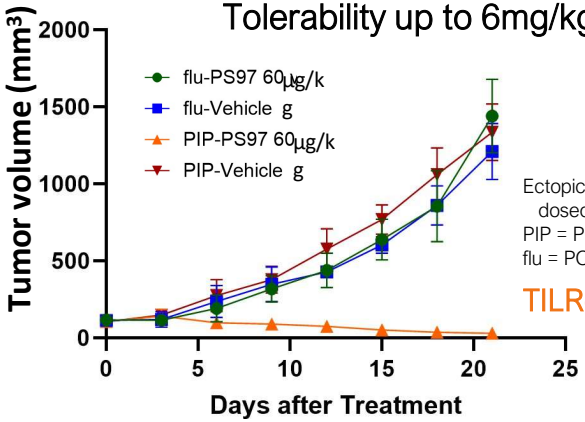
Rob Flavell, MD, PhD
Assoc. Professor, UCSF Radiology

Jeff Neitz, PhD
Assoc Dir, UCSF Small Molecule Drug Discovery Center

Rahul Aggarwal, MD
Prof of Medicine, UCSF
Assoc Director, Phase I clinical studies ctr

Eileen McCullough
CEO
Clasp Tx, Vedere Bio I, Tizona, Potenza MRL Ventures

Lead Program Shows Anti-tumor Efficacy at 60µg/kg, Tolerability up to 6mg/kg in mice



Ectopic PC3-pip xenograft, male NSG mice dosed qd 60 µg/kg
PIP = PC3-PIP high PSMA-expressing cell line
flu = PC3-flu low PSMA-expressing cell line

TILR-097-treated

DISEASE/INDICATION: Prostate, breast, ovarian, other solid tumors

UNMET NEED: not an ADC – ADCs deliver <1% of drug to solid tumors, have narrow therapeutic indices, dose-limiting toxicities, long serum half-life, and premature payload loss. SMDCs designed to meet unmet clinical need for targeted therapies with short PK and effective tumor payload delivery alone or in combination with other therapies.

PRODUCT: Small molecule drug conjugates selectively delivered to tumor cells. Multiple potential payloads – MMAE; tecans; PARPi; TLR, PROTACs, etc. Molecular dynamics-based platform approach to design novel ligand-linker-payload combinations in silico with in vitro and in vivo lead candidate selection. Based on 3 yrs funded research.

SMDC FORMAT COMPETITIVE DIFFERENTIATION VERSUS ADCs:

- Excellent payload retention in plasma, targeted delivery to tumor, and rapid clearance to limit off-tumor toxicity
- Biomarker: Approved PET imaging agents enable patient selection and progression monitoring
- Lower cost-of-goods, standard community-enabled administration

DATA:

- PS-97 asset IND (2H2025); pilot canine, murine tox complete
- Second PS-133 asset one year behind
- Proprietary methods established to enable targeting other malignancies previously de-risked by ADC / RLT activities

TIPPINGPOINT BIOSCIENCES

Pioneering a Solution for Diseases of DNA Packaging Dysfunction

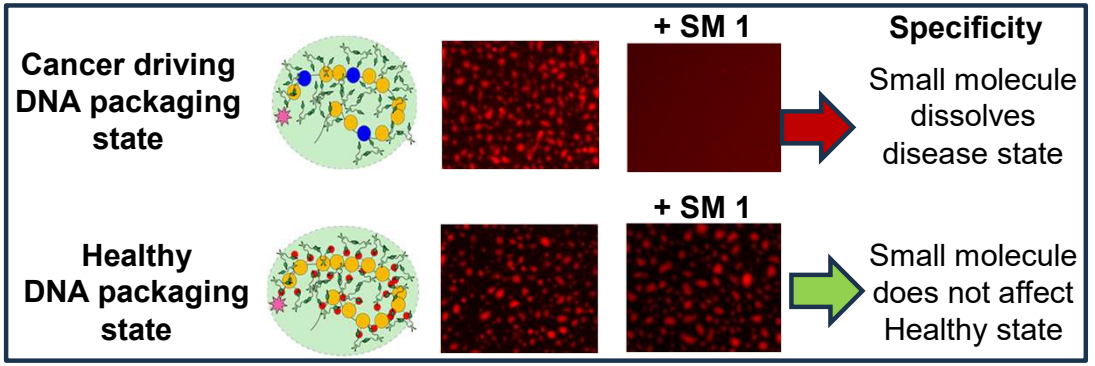
UCSF

Geeta Narlikar, PhD
Co-Founder, TippingPoint
UCSF Professor, Member
National Academy of Sciences

Laura Hsieh, PhD
Co-Founder and CEO,
TippingPoint Biosciences
American Cancer Society Postdoc
Fellow, UCSF

PROBLEM:

- Cancers arise from aberrant DNA packaging.
- Current therapeutics target *single* defective factors not the *entire* aberrantly packaged state.
- Approaches to target entire aberrantly packaged DNA states can broaden cancer treatment and reduce potential for resistance.



SOLUTION:

- TippingPoint's platform synthetically generates disease and healthy DNA packaged states
- Readily scalable for small molecule screening
- Allows for the first time, drugging of entire disease driving DNA packaged states, with high specificity
- Applications in cancer and regenerative medicine

TRACTION:

- >$1.7M in pre-seed fundings from MBC Biolabs, IndieBio (SOSV), ACS BrightEdge
- Won Abbvie Golden Ticket, ONO Pharma Golden Ticket & Astellas Future Innovator Award

LEARN MORE:

Treating drug-resistant prostate cancer by targeting PTGES3

Luke Gilbert, PhD
UCSF Associate Professor, Urology

Felix Feng, PhD
UCSF Professor, Radiation Oncology, Urology, Medicine

Kevan Shokat, PhD
UCSF Professor, Cellular, Molecular Pharmacology

DISEASE/INDICATION: Prostate cancer

UNMET NEED: Nearly all mortality in prostate cancer is due to metastatic castrate resistant prostate cancer (mCRPC). Regulating androgen receptor expression could reinstate drug sensitivity.

PRODUCT: PTSGE3 targeting small molecules

COMPETITIVE ADVANTAGE/DIFFERENTIATION:

- Metastatic androgen receptor (AR)-driven prostate cancers develop resistance to existing FDA approved drugs targeting AR signaling.
- New androgen receptor-inhibitors could possibly overcome mechanisms of drug resistance

DATA: POC data supporting leads

Woodwinds Therapeutics

A Drug Discovery Paradigm to Fast-Track Adaptation to Hypoxia

UCSF

Lani Wu, PhD and
Steven Altschuler, PhD
Co-founders, Woodwinds Tx
Professor, Dept of Pharmaceutical Chemistry

Matthew Jacobson, PhD
Co-founder, Woodwinds Tx
Professor, Dept of Pharmaceutical Chemistry

PROBLEM:

- Drug discovery efforts for hypoxia indications have been challenging because of complex underlying mechanisms.
- Current standards of care in anemia in chronic kidney disease are effective but have significant safety concerns.

SOLUTION:

- Combined AI-enabled *in vivo* and *in vitro* platform to **uncover novel oxygen disease targets and therapies that fast-track adaptation.**
- First clinical program: targeting anemia in CKD
- In vitro POC and pilot screen performed, and hits identified.
- Multiple promising oxygen disease targets discovered.

TRACTION:

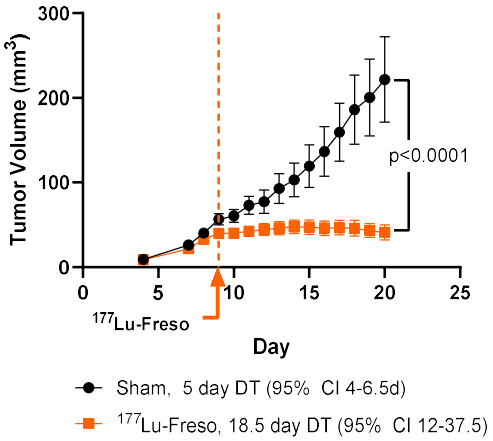
- $14M in DARPA funding
- Published tool compound for anemia in CKD target increases EPO only during hypoxia

LEARN MORE:

XRX: A Tunable TGFβ Theranostic

Mary Hellen Barcellos-Hoff, PhD
Professor, Radiation Oncology, UCSF
World-renowned expert in TGFβ

Henry VanBrocklin, PhD
Professor, Radiology, UCSF
World-renowned expert in radiopharmaceuticals



DISEASE/INDICATION: Glioblastoma, lung cancer, breast cancer, Head and neck squamous cell carcinoma (HNSCC)

UNMET NEED: Need for more radiopharmaceuticals (RPTs):

- Promising modality for precision cancer treatment.
- Treatment can be personalized based on target imaging.
- RPTs are only approved for 7% of all cancers.

Need better strategy to target TGF β

PRODUCT: repurposing Fresolimomab (a monoclonal antibody that binds to the active form of human TGFβ1, TGFβ2, and TGFβ3 by adding ^{89}Zr for PET imaging and ^{177}Lu for treatment

COMPETITIVE ADVANTAGE/DIFFERENTIATION:

- First tumor agnostic RPT
- TGFβ activity is continuously high in tumors and low in normal tissue
- TGFβ activity is further increase by radiation
- Instead of inhibiting TGFβ activity, we are using TGFβ to localize radioisotopes
- Radiation can't reach many metastatic disease sites, this RPT can
- Repurposing of validated, off patent agents with high specificity at a much lower systemic dose

DATA

- ^{89}Zr-Freso localizes to tumors. Update is increased by irradiation
- ^{177}Lu-Freso reduces tumor volume (shown)