SPARK Colorado Therapeutics Pipeline -

- Target Validation
- Lead Optimization
- Pre-clinical
- Phase 1

Legend:
- Biologic
- Small Molecule
- Cell Therapy

- EGF Fusion-Toxin - Oncology
- AMPs - Gram Negative Infections
- CaMKII - Neuroscience
- SMAD7/TGFβ - Ophthalmology
- AMPD - Metabolic
- AMPI-109 - Oncology
- TOP2A - Oncology
- AMPK - Oncology
- SIX1 - Oncology
- CtBP - Neuroscience
- HDAC6/8 - Cardio
- Autologous CD117+ - Organ Transplant
- Engraftable HSCs – Immunology
- iPSCs - Cardiomyopathy
- Retinal SCs - Ophthalm.

Program Details
- Milestone based funding
- 10 projects per cycle accepted
- Industry and EIR advisors
- Mentorship and training

Currently supporting 28 therapeutic, diagnostic, and medical device projects
Aurora Oncology

**Problem**
Bladder cancer recurrences are common and lead to devastating treatments or death. Highest lifetime cost/patient of any cancer.

**Solution**
DT-EGF - Epidermal Growth Factor (EGF) targets diphtheria toxin A (DT) to bladder cancer cells without harming healthy cells.

**Advantages**
- Prior human clinical trial data
  - IV route – Solid tumors
- Proven efficacy in animal models of bladder cancer
  - Intravesical route
- Strong IP
  - IP awarded: WO2011047135A3
  - Provisional filed: 62/837,533
- Clear FDA guidance
  - Small clinical trial size for approval

**Development Status**
- NIH-Fastrack awarded
- DTEGF production ongoing
- Animal models est. PD/PK/TK
- Pre-IND meeting planned.

Inventors: Thomas Flaig, Arthur E. Frankel, Andrew Thorburn, L. Michael Glode, Jung Hee Woo, David Neville

Departments: Medicine, Pharmacology
Designing Antimicrobial Peptides (AMPs) with no toxicity as novel therapeutics targeting Gram-negative pathogens

**Problem**

There is a worldwide crisis of Gram-negative pathogens resistant to all available antibiotics including antibiotics of last resort, polymyxin B and colistin.

**Solution**

Designed de novo amphipathic α-helical antimicrobial peptides (AMPs) containing specificity determinants ensuring specificity towards bacterial cells over eukaryotic cells.

Utilize non-standard amino acids on the polar face (diaminobutyric acid residues, Dab, and diaminopropionic acid residues, Dap) eliminating toxicity.

**Advantages**

- Our AMPs are completely resistant to proteolysis or enzymatic degradation which prolongs half-life for systemic drugs.
- AMPs have no measurable toxicity to human red blood cells with non-standard amino acids.
- No significant binding to serum proteins.
- Strong IP portfolio.

**Development Status**

- Developed rat model to test biological activity of AMPs.
- Screening lead compounds for cytotoxicity against a series of human primary cells.
- Screening toxicity and pharmacokinetics (PK) studies on our lead compounds in rats.
- Developing GMP manufacturing process.

Inventors: R.S. Hodges, C.T. Mant, L. Gera

Department affiliations: Biochemistry and Molecular Genetics

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**First In Class Therapeutic for Neuro-Protection After Ischemia**

**Problem**
No drug to treat neuronal cell death after cerebral ischemia.

stroke: focal cerebral ischemia 795,000/yr (United States)

GCI: global cerebral ischemia 360,000/yr (United States)

**Solution**
Highly selective peptide inhibitor (tatCN19o) targeting CaMKII.

- Cerebral ischemia triggers CaMKII-induced neuronal cell death
- Therapeutic given via injection within 1-hr of injury

**Advantages**
- No current competitor
- Genetic corroboration of the mechanism
- Target downstream of NMDA receptors (improving time window)
- Protects from both cell death and impairments of the surviving cells
- Works in combination with standard of care (therapeutic hypothermia)
- Animal proof-of-concept complete
  - Efficacious in non-rodent model
  - Tested in highly relevant cardiac arrest (CA)/CPR model

**Development Status**
Demonstrated *in vivo* efficacy in mouse; indicated also in pig

Preliminary safety studies raised no concerns.

Ulli Bayer & Steven Coultrap
Department of Pharmacology

Paco Herson  (neuronal injury)
Vik Bebarta  (pig model)
Jost Klawitter  (PK analysis)
**Problem**
Effective treatments are needed to prevent ocular fibrosis that can lead to vision loss.

**Solution**
We are developing novel mechanism-based inhibitors to block fibrosis of the retina and lens.

**Advantages**
- Inhibitors target molecular pathways
- Dual inhibitor strategy
- Current clinical need involving >20 million cases/yr worldwide

**Development Status**
- Proof of concept studies in cell culture and animal models.
- Optimizing formulation strategies.

Mark Petrash PhD,
Xiao-Jing Wang MD, PhD
Ophthalmology; Pathology and Dermatology

Mark.Petrash@Cuanschutz.edu
Colorado Research Partners, LLC : Developing treatments for Nonalcoholic Fatty Liver Disease (NAFLD)

**Problem**
Non alcoholic liver fatty liver disease (NAFLD) is the most common type of liver disease, is driven mainly by sugar intake, and there is no currently effective treatment.

**Solution**
We have developed orally active, potent, selective inhibitors of sugar (fructose) metabolism blocking NAFLD.

**Advantages**
- Treats the cause of NAFLD and not downstream signals
- Humans lacking target enzyme in fructose metabolism are healthy
- Prevents type 2 diabetes, lowers BP and improves dyslipidemia
- May block certain cancers (pancreas)

**Development Status**
- Lead compounds at preclinical stage
- Patent protected
- Currently working on development candidates for phase I

Inventors Richard J Johnson, Miguel Lanaspa, Michael Wempe
Department affiliations: Medicine, Pharmacology

Richard J Johnson MD
Richard.Johnson@ucdenver.edu
AMPI-109: A Breakthrough Therapy for Triple-Negative Breast Cancer

**Problem**
Triple-negative breast cancer is an aggressive disease with a high propensity to metastasize and relapse; there is a critical medical unmet need for new therapies.

**Solution**
The inventors have characterized the use of the small molecule drug AMPI-109, which has a low toxicity profile and mechanism of action distinct from current pipeline drugs.

**Advantages**
- Low toxicity
- High potency
- Orally available
- Biomarker guided
- Broad cancer indications

**Development Status**
- Completed - *in vitro* efficacy and target identification
- Current: *in vivo* efficacy & PK/PD
- Establishing new startup company: Vona Oncology, LLC

James Lambert, Hamid Gari*, Scott Lucia, Ann Thor, Rahul Ray#
UCD Pathology, *Hoffmann-La Roche, #Boston University

jim.lambert@cuanschutz.edu
**Problem**

EMT is a driving force in tumor progression that transforms benign epithelial cells into mesenchymal cells, promoting drug resistance, invasion and increased metastasis.

**Solution**

Small molecules that reverse EMT making malignant mesenchymal cells revert to a more benign cell state and susceptible to standard therapeutics again.

**Advantages**

- EMT targeting drugs slows primary tumor growth
- Therapeutics inhibit metastasis
- EMT targeting drugs may extend survival rate $\geq 5$ years
- Combo therapies with EMT drugs will sensitize primary tumors and metastatic lesions.

**Development Status**

*In Vivo* Studies In Progress: Combination studies with clinical drugs, ADME, PK and toxicology, anti-metastasis efficacy studies.

Dan LaBarbera, PhD
Department of Pharmaceutical Sciences Skaggs School of Pharmacy

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Targeting AMPK in Glioblastoma

**Problem**
Despite intensive treatment and new experimental therapies the prognosis for GBM patients remains poor.

**Solution**
GBM and GBM stem-like cells (GSCs) are highly dependent on the metabolic regulator AMPK for survival.

**Advantages**
- Currently there are no potent and selective AMPK inhibitors
- AMPK inhibition may sensitize GBM cells to chemotherapy
- AMPK inhibition has the potential to eliminate GSCs

**Development Status**
Developed novel small molecule nanomolar AMPK inhibitors and demonstrated cellular target engagement.

Inventors: Philip Reigan, PhD
Department affiliations: Pharmacy

philip.reigan@cuanschutz.edu
Targeting the Six1-Eya Complex to Inhibit Metastasis

Problem
Metastasis is the major cause of death for cancer patients, yet to date drugs often do not target metastases. Current treatments are limited in preventing continued metastases from the primary and secondary tumor sites.

Solution
Developing novel protein interaction inhibitors targeting the Six1/Eya protein complex interface. Disrupting this transcriptional complex inhibits breast cancer metastasis.

Advantages
- Target metastases, the major killer of cancer patients
- Six1/Eya have low expression in healthy tissue, thus inhibitors will have limited side effects
- Inhibitors target a transcriptional node driving tumor cells as opposed to upstream targets (e.g. kinases), thus limiting resistance mechanisms.

Development Status
Complete: \textit{in vitro} and \textit{in vivo} proof of concept experiments
Next: optimize lead compound

Heide Ford PhD and Rui Zhao PhD
Departments of Pharmacology and Biochemistry & Molecular Genetics

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Therapeutic Targeting of Neuroinflammatory Transcription In Mild Traumatic Brain Injury (TBI)

**Problem**
There is no clinical treatment for mild TBI despite its increasing prevalence and economic burden due to chronic neurological impairments.

**Solution**
Mechanism-based small-molecule modulators of TBI-triggered neuroinflammation.

**Advantages**
- Novel molecular target for TBI.
- New compounds inhibit TBI-induced inflammatory responses.
- Efficacy proven in animal studies against inflammation and neurologic deficits caused by mild TBI.

**Development Status**
- Identify effective time window and dose of intervention in vitro.
- In vivo assessment of ideal intervention time window and effect.

Mingxia Huang, PhD
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Targeting a Myofibril Post-translational Modifications to Treat Heart Failure

**Problem**
Millions of people suffer from heart failure (HF), and the 5-year mortality rate for these patients is ~50%, highlighting an urgent unmet medical need.

**Solution**
We have devised an innovative approach to treat HF based on manipulation of an enzyme that controls the stiffness of myofibrils, which are the major contractile units of the heart.

**Advantages**
- First therapy to target stiffness of the heart via a myofibrillar protein and major regulator of dilated cardiomyopathy (DCM) and HF with Preserved Ejection Fraction (HFpEF)
- Novel target for HF
- Class of inhibitors shown safe in humans for other indications

**Development Status**
*In vivo* validation of tool inhibitor in a rat model of genetic DCM

Timothy McKinsey, Ying-Hsi Lin, Kathleen Woulfe, Maria Cavasin, Keith Koch

Medicine/Cardiology

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Autologous CD117+ Progenitor Cell Therapy for Solid Organ Transplantation

**Problem**
70% of Lung transplant patients have at least 1 episode of acute rejection 30% develop chronic rejection by 3 years

**Solution**
An autologous stem cell therapy:
- prevents acute rejection
- may decrease immunosuppressive needs and morbidities
- may promote allograft tolerance
- increases graft survival

**Advantages**
- CD117+ cells can be mobilized to peripheral blood in preparation for positive-selection apheresis, collection and storage.
- Little risk of sensitization
- No rejection of the cells
- No graft vs host disease
- Confirmed freedom to operate

**Development Status**
In a murine heart transplant model, systemically administered CD117+ bone marrow derived progenitor cells attenuate acute rejection. International patents granted

Marty Zamora MD, Rob Plenter, & Todd Grazia MD
Department of Medicine

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Generation of engraftable hematopoietic stem cells from induced pluripotent stem cells

Problem
Bone marrow transplant is highly risky to treat leukemia, lymphoma and genetic bone marrow failure disorders.
Only 1:3 patients have a viable donor for bone marrow transplantation.
Induced pluripotent stem cells show promise but are not able to engraft into patients.

Solution
Developed novel process to create bone marrow stem cells that are engraftable for the patient.

Advantages
- Autologous transplantation eliminating problem of finding a donor (mismatching/GVHD)
- Safer than viral modification
- Small molecule is already approved by FDA (different indication) – proven safety
- Easy to apply to human studies

Development Status
- Identified engraftable HSC with the small molecule.
- Future work:
  1. Serial engraftment
  2. How does the drug influence engraftment?

Michael Verneris, MD
Sunny Shim, PhD
Pediatrics – Heme/Onc

< Harvard group, Nature 2017>

Lentivirus infection
Overexpression of 7 genes

Murine engraftment

< Our strategy>

Bone Marrow Transplant: Replacement of diseased or damaged bone marrow

IPS/HEK cell
Off the shelf Cell therapy

HSC(hematopoietic stem cell)
Multi-lineage lymphocyte

Epigenetically increased expression of 7 genes
Additional effect: Expansion of Hemopoietic Stem Cells

Murine engraftment

Small Molecule
Heart Regeneration by Conversion of Cardiac Fibroblasts to Cardiomyocytes

**Problem**
Heart attack increases numbers of cardiac fibroblasts, but causes cardiomyocyte death which have limited regenerative capacity.

**Solution**
Reprogramming of cardiac fibroblasts into cardiomyocytes for heart regeneration using viral-based gene delivery in combination with pro-fibrotic inhibitors.

**Advantages**
- No cell-transplantation.
- Reduction in cardiac scar.
- Regenerate cardiomyocytes from cardiac fibroblasts *in situ*.
- Excellent team: translational scientists and clinical leaders in cardiology.

**Development Status**
Carrying out proof-of-concept *in vivo* in disease animal model
Patent# 9,885,018 – 2/6/2018: High Efficiency Reprogramming of Fibroblasts Into Cardiomyocytes Requires Suppression of Pro-Fibrotic Signaling

Inventors: Kunhua Song PhD, Peter Buttrick MD, Yuanbiao Zhao PhD
Department affiliations: Cardiology
Stem cell-derived 3D retinal transplant to treat dry AMD

**Problem**
AMD is the leading cause of irreversible blindness worldwide and there is no available treatment for these patients.

**Solution**
Our product is a retinal transplant generated from human stem cells, that recreates the organization and function of the retina, and is designed to restore vision by regenerating the retinal cells loss to disease.

**Advantages**
Our product has the potential to be the first treatment for dry AMD, targeting an estimated $30 million global market, with more than 20 million patients worldwide immediately eligible to receive our retinal transplant.

**Development Status**
Initiating *in vivo* proof-of-concept studies.

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SPARK Colorado Medical Device & Diagnostic Pipeline

Currently supporting 28 therapeutic, diagnostic, and medical device projects

Program Details
- Milestone based funding
- 10 projects per cycle accepted
- Industry and EIR advisors
- Mentorship and training
The “Button Huggie”

Problem
No product on market to secure gastrostomy buttons and reduce tract-related complications, such as granulation tissue formation, peristomal leakage and accidental dislodgement.

Solution
Small, precision designed, low profile gastrostomy button securement device composed of replaceable gauze sponge, disposable base layer and reusable lid.

Advantages
- Easy gauze replacement
- Internal structure:
  - Centers base layer around button
  - Reduces movement in tract
  - Supports button when attaching extension feeding tube
- Prevents dislodgement

Development Status
Injection molder and converter identified, e-commerce website and QMS in development, 510(k) exempt

Inventors: Moulton, Mironuck, Fried, Heckman
Departments: Surgery and Mechanical Engineering
Implantable Device for Dry Macular Degeneration

**Problem**

Dry Age Related Macular Degeneration (AMD) represents 90% of AMD cases and a leading cause of visual deterioration. There are zero effective treatments for dry AMD.

**Solution**

A medical device that is implanted into the vitreous to absorb and filter proteins that drive the progression of dry AMD.

**Advantages**

- Easily implanted during a single office procedure
- Once device is saturated with deleterious proteins, it can be easily cleaned without removal
- Inexpensively manufactured

**Development Status**

Complete: *in vivo* proof-of-concept

Patents Pending

Next: Complete GMP production for first in human clinical study

Jeff Olson, MD
Ophthalmology

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Problem
Vascular access in a pre-hospital setting is extremely difficult with high morbidity

Solution
VASAFAST: A novel, semi-automatic, user friendly medical device that guarantees safe vascular access.

Advantages
• Obtain vascular access in less than 25 sec compared to the current 10 min.
• Field use ready, experienced clinicians not required.
• ‘One part’, portable, and compact.
• Novel means to identify vessels.
• The stability rig holds the needle cartridge steady even during CPR

Development Status
Prototype developed, cadaver tested, customer/market reviewed

Juan-Pablo Idrovo and Andrew Scallon
Department of Surgery / Department of Physiology and Biophysics

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LVAD Apical Cuff implantation device

**Problem**
Increased operative time and bleeding are associated with Apical Cuff placement during Left Ventricular Assist Device implantation

**Solution**
Develop a surgical device to automate LVAD Apical Cuff implantation

**Advantages**
- Reduced operative time
- Reduced bleeding / morbidity
- Facilitate implantation through minimal access incisions

**Development Status**
- Large animal prototype stage
- Multiple pending patent applications
  - Notice of allowance received for method of treatment claims

Inventor: Max B. Mitchell, MD
Department of Surgery
**Problem**

Spinal fusion cages can break through the vertebral end plate causing the patient severe pain and disability.

**Solution**

Design a patient specific spinal fusion cage that matches the stiffness and shape of the vertebral end plate.

**Advantages**

- Significantly reduced chance of subsidence resulting in improved outcomes.
- Reduced risk of a second surgery.
- Implanted with intraoperative imaging guidance for optimal placement.

**Development Status**

- Patent application filed.
- Prototype being tested.
- FDA Q – Submission in progress

Dr. Burger, Dr. Ma*, Dr. Patel, Dr. Kleck, Dr. Noshchenko. T. Baldini

Department of Orthopedics, * U Va.
The Phosfilter is a novel adsorbent medical device developed to reduce uncontrolled phosphate levels in blood and tissues, which are associated with cardiovascular disease in kidney disease patients on hemodialysis.

A single use, disposable device, the Phosfilter consists of phosphate adsorbent microparticles on a medical grade, blood compatible material backing, coiled, within housing unit.

Device will be used during standard hemodialysis

Enhancement in compliance as a phosphate reduction treatment

Improvements in phosphate binding capacity over oral binders

Reduction in complications / side effects over existing oral binders

Reduction in healthcare costs associated with poor phosphate control

Complete: benchtop studies for safety, efficacy, and scalability

Complete: Healthy canine study demonstrating safety

Ongoing: Clinical canine study demonstrating efficacy

Ongoing: Regulatory strategy plan

Melanie S. Joy, PharmD, PhD (U. of CO Skaggs School of Pharmacy)

Marian G. McCord, PhD (North Carolina State University, College of Environmental Resources)

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ESCAPE: External Stereotactic Cranial Access Port for Evacuation

**Problem**
No currently available comprehensive system for bedside evacuation of common intracranial pathology to treat hemorrhage stroke patients.

**Solution**
Frameless stereotactic port which secures to the skull and enables accurate catheter delivery to chosen targets and subdural hematoma evacuation (brain bleeds).

**Advantages**
- Accurate/safer procedures (goal)
- Bedside procedure / no operating room required
- Significant cost reduction
- MRI compatible device

**Development Status**
- Provision patent filed
- Advanced prototype made
- Strength testing done
- Road to market analysis pending

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Bioresorbable 3-D Printed Personalized Implant for Cartilage Regeneration in Pediatric Growth Plate Injuries

**Problem**
Growth plate injuries can stunt bone growth in children, and current treatments are <30% effective.

**Solution**
3D printed personalized implant that regenerates injured tissue and biodegrades as the child grows.

**Advantages**
- Personalized to patient
- Mechanically stable
- Regenerates damaged tissue
- Grows with the child
- Possible FDA Humanitarian Device Exemption

**Development Status**
Testing in rabbit model of growth plate injury
PCT International App filed November 6, 2018

Karin Payne, PhD1; Nancy Hadley Miller, MD1; Stephanie Bryant, PhD2; Virginia Ferguson, PhD2
1 Department of Orthopedics, CU Anschutz
2 School of Engineering, CU Boulder

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Novel Drug Delivery System to Eradicate Urinary Tract Infections

**Problem**
Urinary tract infections affect 150 million people/year and cost ~$2.6 billion annually in the US due to their ability to create intracellular biofilms that shield bacteria from destruction and facilitate recurrent infections.

**Solution**
Target delivery of antibiotics directly into bladder cells using nanotechnology to eradicate urothelial biofilms and kill bacteria.

**Advantages**
- Prevent multidrug resistance
- Avoid intravenous antibiotics
- Decrease hospitalization rates
- Reduce healthcare costs
- CPT coded for reimbursement

**Development Status**
- Formulated nanogels loaded with therapeutic antibiotic doses
- Demonstrated effective, dose-dependent killing of bacteria by antibiotic-loaded nanogels *in vitro*
- Confirmed ability of nanogel to stably bind to and enter bladder urothelium

**Inventors:** Marsha K. Guess, MD, MS², Kathleen A. Connell, MD¹, Devatha Nair, PhD², Dmitri Simberg, PhD³, Michael Schur⁴

**Departments:**
1. Obstetrics and Gynecology; 2. Craniofacial Biology; 3. Pharmaceutical Sciences; 4. Immunology & Microbiology

**Contact:**
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**Problem**

Head and neck cancer is one of the most common forms of cancer with 650,000/yr cases worldwide and ~50M individuals classified as high risk (e.g. cigarette and alcohol use).

There are no effective early detection methods.

**Solution**

Developed a molecular based assay to detect a novel genetic biomarker for H/N cancer from a saliva sample.

**Advantages**

- Non-invasive saliva-based sample acquisition.
- More sensitive and cost effective than currently diagnostic methods (e.g. MRI)
- Proprietary algorithm to analyze genetic signature.

**Development Status**

Testing effectiveness for head/neck cancer recurrence.

SummitDx – startup formed

Shi-Long Lu, MD, PhD
Department of Otolaryngology
Surrogate Molecular Assessment of Response to Treatment of Tuberculosis (SMART-TB)

Problem
There is currently no pharmacodynamic marker of tuberculosis drug regimen efficacy. Many tuberculosis drug regimens look promising by measurements of bacterial burden but ultimately fail to prevent relapse.

Solution
We developed a novel biomarker to assess the physiological state of M. tuberculosis during drug treatment and to predict the likelihood of a drug regimen to prevent relapse.

Advantages
• Fills crucial gap in assessment of tuberculosis regimens by addressing bacterial physiological state instead of pathogen burden
• Exquisitely sensitive – valid measurement that requires low numbers of bacteria
• Rapid analysis of new regimens – normal mouse validation requires 18 months
• Potential for stratified tuberculosis treatment

Development Status
• Provisional patent, PCT filed
• Currently validating biomarker on M. tuberculosis regimens in vitro, in mice, and in humans
• Beginning the process to Qualify biomarker through FDA

Nicholas Walter, Martin Voskuil, Gregory T. Robertson, Sarah Born
University of Colorado Anschutz Medical Campus
Colorado State University
**Problem**

- Traumatic injury causes **180,000 deaths** annually in the US alone, primarily from uncontrolled bleeding and trauma-induced coagulopathy (impaired blood clotting).
- Current clinical laboratory tests to assess blood coagulation are based on 70-year-old technology, are slow, and provide incomplete information.
- Thus, a critical gap in current medical technology is the ability to rapidly and accurately assess coagulation for the purpose of trauma triage.

**Solution**

- The **tPA-Challenge™** assay uses the “clot busting” agent tPA to rapidly provoke and measure clot breakdown in an injured patient’s blood sample.
- This tests the physiologic reserve of that patient’s coagulation system and predicts their risk of decompensation and massive hemorrhage.

**Advantages**

- The **tPA-Challenge™** is the *only* diagnostic assay capable of scene-of-injury triage.
- Yields results 30-60 minutes faster than existing assays.
- Runs on standard analyzer platforms available at most hospitals.
- Inexpensive, at <$50 per assay.
- Reimbursable under digital health CPT codes.

**Development Status**

- Clinically validated in >900 trauma patients.
- Currently marketed for research use only.
- Shovel-ready for FDA/pivotal trial.

**Inventors**

Michael P. Chapman MD, Vascular and Interventional Radiology
Hunter B. Moore MD PhD, Transplant Surgery
Ernest E. Moore MD FACS, Trauma and Acute Care Surgery

**Primary Contact**

Michael P. Chapman MD
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Detection of Synthetic Drugs of Abuse

**Problem**
Synthetic cannabinoid use is (1) increasing, (2) not detectable using standard antibody based technologies, and (3) causing dangerous medical side effects.

**Solution**
Developing diagnostic assay detecting patients abusing synthetic forms of cannabis.

**Advantages**
- A cell based assay can be used in a reference laboratory.
  - Military & law enforcement to be first clients.
  - Far cheaper than mass spectrometry alone.
- Creating a point-of-care assay to be used in an emergency room setting.

**Development Status**

Andrew Monte\(^1\) and Robert Scheinman\(^2\)

\(^1\)Department of Emergency Medicine, School of Medicine \(^2\)Department of Pharmaceutical Sciences, School of Pharmacy. CU Anschutz.