Intelligent Optical Systems, Inc.

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Tac-Assay *in vitro* Diagnostic:

Tacrolimus Enhanced Lateral Flow Assay (eLFA) Business Opportunity

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Acknowledgement and Disclaimer

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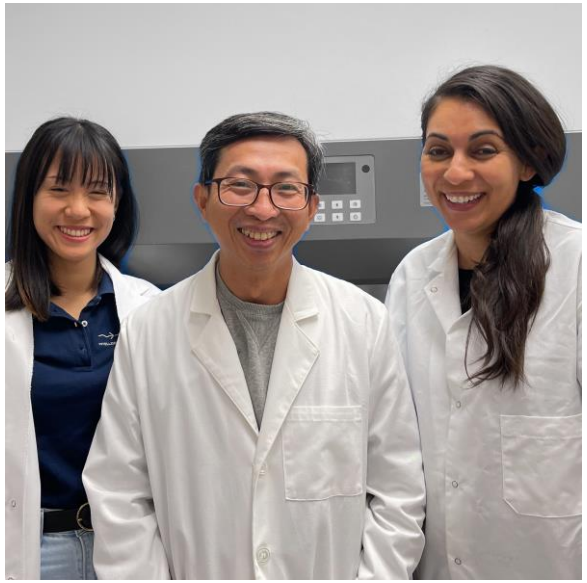
- Any opinions, findings and conclusions or recommendations expressed in this material are those of the author(s) and do not necessarily reflect the views of the U.S. Army Medical Research and Development Command (USAMRDC).

About IOS and MISAA

The seasoned scientists at IOS focus on creating & optimizing sensing at levels of competence not normally seen in industry. Their unique depth and breadth of scientific expertise has enabled IOS to solve complex physical, chemical, biological, and optical challenges and convert them to extraordinary products.



The scientists are driven to succeed by their shared passion for knowledge and growth, and the desire to apply that knowledge to remedy real-world problems, from healthcare to environmental sustainability.

The Tacrolimus eLFA will bring improved quality of life "to the fingertips" of transplant recipients worldwide.

IOS has spun out MISAA, LLC (Monitoring Immunosuppressants Anywhere Anytime)

- MISAA, LLC contains the IP for the Tac-Assay and has an operating agreement with IOS to use its scientists, facility, etc.

As you will read, the MISAA Tacrolimus eLFA is a groundbreaking technology that:

- When fully funded and deployed, will have significant impact on the world transplant community; and
- Will bring greatly improved quality of life "to the fingertips" of transplant recipients worldwide.

Business Proposition

The Problem

- Tacrolimus (Tac) is an essential immunosuppressive drug for solid-organ and tissue transplant patients

- Frequent patient monitoring is critical – Tacrolimous has a short therapeutic window that differs widely between individuals – too high a level causes drug toxicity, too low a level causes transplant rejection. Chronic rejection is becoming more of a problem; one key solution suggested is tighter control of immunosuppressant levels.

- Current monitoring is by frequent venous blood draws measured with LC-MS/MS. Testing is painful, complex and costly. Limitations on same-day turnaround can compromise effective dose adjustments.

The Solution

- Tac-assay has been validated against LC/MS-MS with 54 kidney transplant recipients in a hospital setting to date
  - Strong interrelationship – Pearson correlation r = 0.89
  - Good agreement – Bland-Altman analysis mean bias = 0.7 ng/mL at 95% limit of agreement.

- Over the past three years, IOS has developed and patented (pending) an eLFA for rapid, accurate, reliable and highly sensitive point of care monitoring of tacrolimus levels in capillary blood from fingerstick
  - Enables clinicians to adjust ISD levels on the order of minutes rather than hours or days
  - Less invasive and user friendly for patients, leading to improved patient outcomes.

Pains in the Existing Transplant Marketplace

- Hospital systems' incentive to reduce costs
- Hospital and outpatient labs crowded
- Monitoring is complex and demanding
- Transplant failure

Patient Non-compliance to Protocols

- Restrictive testing schedules
- Access to testing
- Cost of medication

Ultimate Value Proposition

To Hospitals and Insurance Companies

- **Reduces hospitals' financial burden** by eliminating the need for expensive LC-MS tests, and eases their labor burden by eliminating the need for a specialist and lab staff trained on complex instrumentation, and reduced need for nursing staff
- **Increases patient medication compliance:** Point of Care **"**POC" testing, with its low cost and ease of use, reduces transplant failure "*…rejection and the associated increased immunosuppression burden increase hospitalization rates, healthcare costs, and the risk of dying from cardiovascular disease and cancer …*" [I. Gandofini et al. "Detecting, preventing and treating non-adherence to immunosuppression after kidney transplantation" Clin Kidney J 2022] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9217626/
- **Lower insurance costs:** Successful transplant recipients, when properly supported by the healthcare industry, lead healthier lives. Healthier patients cost less for hospitals, insurers, and the government.

To Physicians and Patients

- **Less invasive:** Fingerstick is much less invasive than blood draw
- **Adjunct to Telehealth:** The clinician can advise the patient on dosage adjustments at point of care. This eliminates the barriers to compliance such as restrictive scheduling of testing, and ease of access for rural and low-income patients.
- **Lower cost to patients:** After 36 months, patients are responsible for the costs of testing
- **Better quality of life:** Successful transplants enable patients to return to a quality of life near pre-disease state
- **Better for future patients:** More successful transplants reduces the overall burden on organ donor wait list.

Progress to Date

Work-to-date funded by $5.3MM of non-dilutive grant money

Round 1 – $402K of SBIR funding

- 09/18/2018 – $252K – Novel Saliva-based Renal Function Test Platform (NIH SBIR Ph I Fast-Track 1R44DK116383-01A1)
- 04/01/2019 – $150K – Enhanced Rapid Assay for Monitoring Immunosuppressant Drugs in Plasma (Army SBIR Ph 1 W81XWH-19-C-0080)

Round 2 - $2.6MM of SBIR funding

- 07/01/2019 – $1.5MM – Novel Saliva-based Renal Function Test Platform (NIH SBIR Ph 2 Fast-Track 1R44DK116383-01A1)
- 08/24/2020 – $1.1MM – Enhanced Rapid Assay for Monitoring Immunosuppressant Drugs in Plasma (Army SBIR Ph 2 W81XWH-20-C-0044)

Round 3 $1.0MM of SBIR funding

- 09/30/2021 – $1.0MM – A Novel Enhanced Lateral Flow Assay (eLFA) Technology for Graft Immunomonitoring in Vascularized Composite Allotransplantation (VCA) (CDMRP/US Army Medical Research Acquisition Activity Award W81XWH2110972)

Round 4 $1.3MM of SBIR Funding

- 03/25/2024 – $1.3MM – A Novel Enhanced Rapid Assay for Monitoring Immunosuppressant Drugs in Whole Blood (DHA/Army SBIR Ph 2 – Contract Number HT942524C0030

IOS Studies & Tac-Assay Performance Results

Technical validation of Tac-Assay eLFA with spiked human whole blood – assessed intra-/inter-assay repeatability on samples spiked with varying levels of tacrolimus. Each sample was measured with five replicates (n = 5) to obtain %CV values. A standard calibration curve was built with n = 3 for each spiked sample to validate the assay in a clinically relevant range, and to interpolate the concentration of tacrolimus from the eLFA readout of clinical samples.

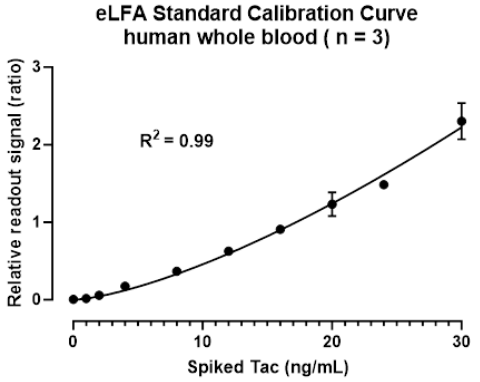
Results: Intra-/inter-assay assessment with spiked human whole blood demonstrated good repeatability, with CV ≤10%. The standard calibration curve indicated the assay performs well in a clinically relevant 0–30 ng/mL range, with a limit of detection of 1 ng/mL.

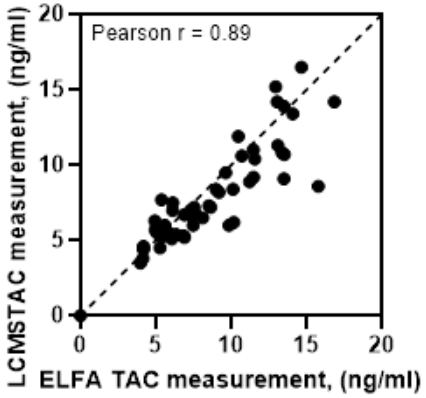
Clinical validations of eLFA and LC-MS tacrolimus measurements – Using Pearson correlation, compared Tac-eLFA measurements (n = 3) of blood obtained via fingerstick from kidney transplant recipients to LC-MS measurements of venous blood collected from the same patient immediately before their next dose of tacrolimus.

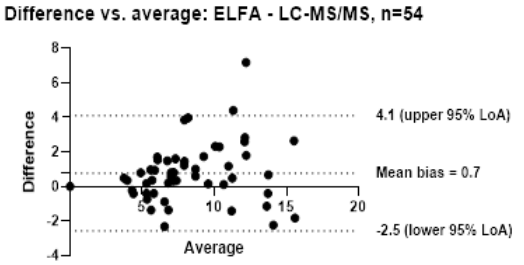
Results: Tacrolimus measurements from 54 clinical samples showed good agreement between the eLFA and LC-MS data sets, with a Pearson score of r = 0.89 and Bland-Altman analysis mean of difference (bias) = 0.7 ng/mL.

eLFA uses dried reagents, which have demonstrated shelf life stability at room temperature storage conditions for more than one year.

Conclusions - The eLFA platform delivers minimally invasive and user-friendly sampling at point of care, and provides rapid, accurate measurements of tacrolimus levels in low-volume blood samples. Results to date obtained from *in vitro* human and *in vivo* clinical blood samples from kidney transplant recipients (n = 54) have demonstrated good repeatability (CV ≤10%) and good correlation (Pearson r = 0.89) with LC-MS standard reference measurements.



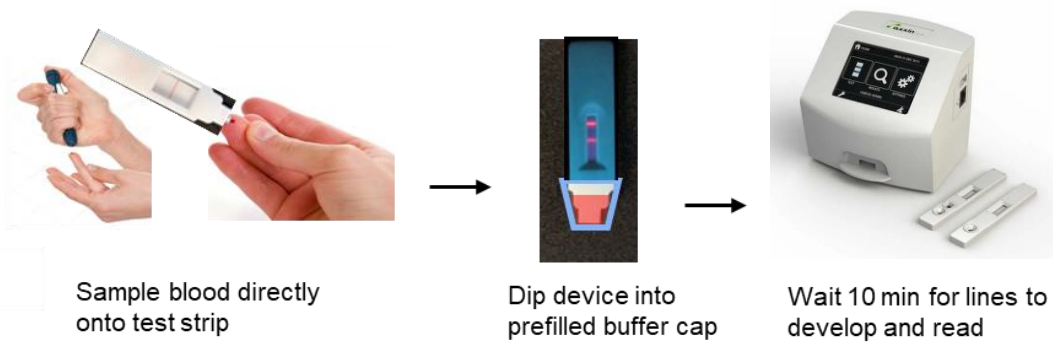




MISAA Tacrolimus eLFA Tac-Assay *in vitro* Diagnostic

Cost-effective, easy-to-use enhanced lateral flow assay for several rapid diagnostics applications featuring:

- **Minimally invasive**, low-volume sampling (fingerstick)
- **Multiplexed** analyte measurement
- **Room temperature storage** for all assay reagents
- **Long shelf-life stability**
- **Enhanced sensitivity** via fluorescent labeling techniques
- **Short test time** <20 minutes



Patent (Pending) Status

- T. Nguyen et al. "Enhanced lateral flow assays and devices for detecting analytes in blood samples," International Application #PCT/US2022/046124, filed 10/07/2022
- T. Nguyen et al. "System and method for quantitative detection of immunosuppressant drugs in whole blood using enhanced lateral flow assay," U.S. Patent Application #63270501, filed 10/21/2021
- T. Nguyen et al. "System and method for assay of tacrolimus in whole blood," U.S. Patent application #63253518, filed 10/07/2021

Next Steps

- October 2023 – 510(k) FDA pre-market submission – complete, Supplemental submission in 90 days

Total Tac Assay Market Size

- Over 92,000 kidney transplants each year worldwide
- 75% of these patients use Tacrolimus, and use it for their whole lives
- 285 average number of tests per transplant
- => 20 million tests per year worldwide
- Reimbursement at $120 times 20 million is $2.40 billion
- Total market growing at 9.5%, will double by 2030

- Revenue from Assay Reader is not included in TAM
- Statistica 2023

Benchmarking

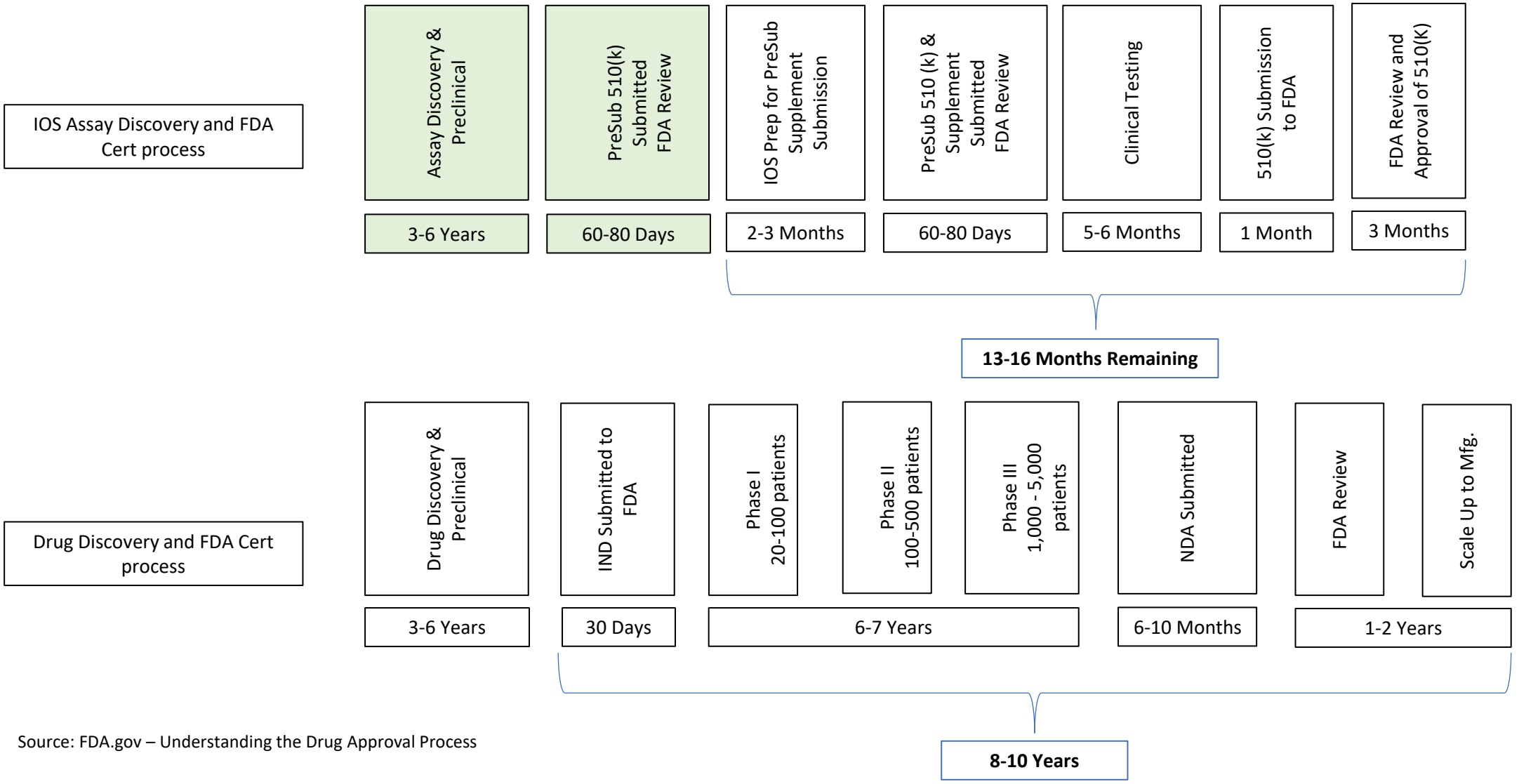
	Tac-Assay eLFA	LC/MS-MS
Price/Test	$120	$139
Blood Vol. Required	5 µL /Fingerstick	1,000 µL /Venous draw
Detection Limit	1 ng/mL	1 ng/mL
Storage	1 year	N/A
Turnaround Time	<15 minutes	12 hours – 3 days
Compatible with Home/POC Testing	Yes	No
Provider	Lab/POC / In-home	Labcorp
FDA Approved/Cleared	In Process	Yes

700248: Tacrolimus, Whole Blood | Labcorp

Business Plan / Revenue Streams

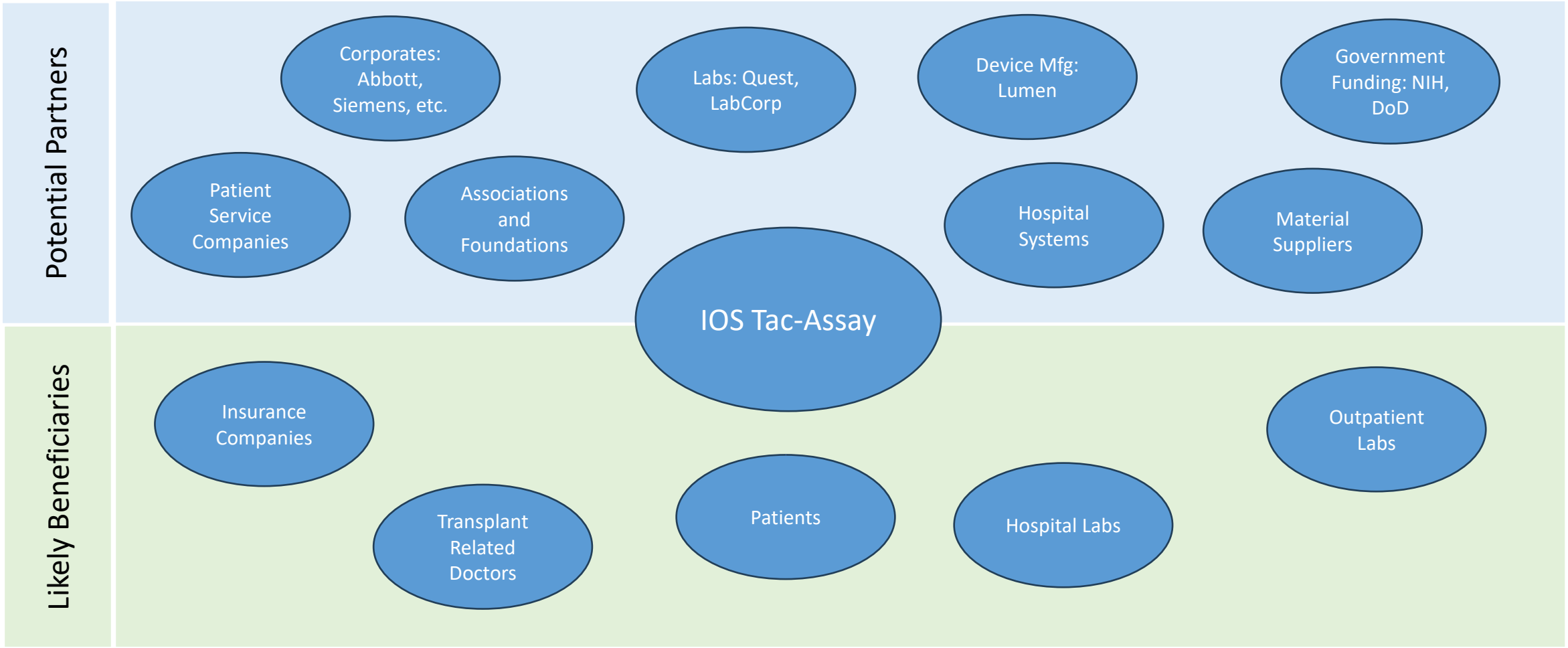
Revenue Stream	Revenue/Price	Type
Test kit w/ reader and initial reagents	~$1,300	One-time payment
Reimbursement	~$120/Test	Billed to Insurance or patient
Resupply of reagents	~$25/Month	Subscription, monthly, etc.
Cloud-based monitoring	~$25/Month	SAAS, subscription, etc.

Tac Assay FDA Approval Process Anticipated to Take 18 months



Source: FDA.gov – Understanding the Drug Approval Process

Tac Assay Transplant Ecosystem



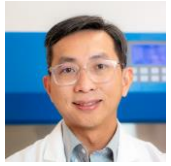
Industry Feedback

Andrew Klein, M.D. Cedars Sinai	"Reducing time between blood draw to test will allow for dose adjustment **in matter of hours as opposed to days**. Lead to better patient outcome."
Irene Kim, M.D. Cedars Sinai	"Home tests are a better market as the doctor's office is equipped with a battery of tests all of which are needed for the doctor to diagnosis"
Vijay Gorantla, M.D., MMM, PhD. Wake Forest	"The sensitivity of the assay is comparable to the **best in the business**."
Kamyar Kalantar, M.D., MPH, PhD. UC Irvine	"Very excited to partner with IOS for the Tacrolimus assay. They see **compelling value** in Tacrolimus and Cystatin C assays."

Team

Joe Gerber – Executive leader with approximately two decades of leadership experience. Possesses extensive experience in building, restructuring and scaling companies. As an executive, he retains specialized knowledge of strategies and company operations that drive growth with proven results in organizational transformation and profit improvement. Mr. Gerber has over a decade of buy- and sell-side M&A investment banking and private equity experience. LinkedIn Joe Gerber

Rahul Ganguli, PhD, CTO – Entrepreneurial materials scientist with twenty years of experience in cutting edge R&D in materials science and product development. Possesses a deep understanding of the pressures and drivers for performing contract research, and the large gap that often exists between government funding and successful commercialization. Dr. Ganguli has been successful in bridging this gap through a relentless focus on the end user, and continuous communication between the major stakeholders. LinkedIn Rahul Ganguli



Trong Nguyen, PhD, Principal Investigator – Leads the team developing novel quantitative lateral flow assays for the detection and measurement of biomarkers and drugs in low-volume whole blood and saliva samples. Developed a proprietary optimal buffer formula for each assay and labeling technique based on DNA hybridization that enhances assay sensitivity to sub-nanogram per microliter or low-picogram per milliliter sensitivity levels. LinkedIn Trong Nguyen

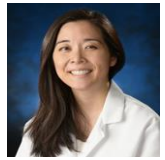
Maria Ortega, MS, Assists in the development of rapid biomedical diagnostic assays using immunochemistry and enzymatic technology including optimizing assay conditions and experimental methods to achieve a working biomedical device for the detection and measurement of various biomarkers. Work includes analyzing data and planning experiments for the screening of material, formulating stability solutions for reagents to achieve an appropriate shelf-life, optimizing assay conditions to improve assay sensitivity and achieve measurements in relevant concentration range. LinkedIn Maria Ortega

Emily Vuu, As a part of the team, optimizes lateral flow assay for detection biomarkers (tacrolimus, interleukin-6, matrix metalloproteinase-3) in blood and saliva samples. Streamlines luminescent, biochemical fiber optic production for electronic blood pressure sensors. LinkedIn Emily Vuu

Scientific Advisory Board

Kamyar Kalantar-Zadeh M.D. – University of California, Irvine – Dr. Kam Kalantar is a triple board certified physician specialist in Internal Medicine, Pediatrics and Nephrology with an MD degree from Germany (Bochum, Bonn, Nuremberg), a Master's degree in public health (MPH), and a PhD in nutritional epidemiology from UC Berkeley, and provides kidney healthcare and consultation in Southern California. He has created the "Harold Simmons Center for Kidney Disease Research and Epidemiology" and "Center of Excellence in Renal Nutrition" with the ultimate goal of longevity and wellness for kidney patients, and to conduct patient-centered studies and train pre- and post-doc students and fellows and early-career investigators. Dr. Kalantar has authored or coauthored more than 1,000 peer-reviewed articles, five textbooks, and many chapters. He is an editor-in-chief, associate editor and editorial board member of many peer-reviewed journals in nephrology and nutrition, and a member of several professional societies.

Vijay Gorantla, M.D. – Wake Forest University – Dr. Gorantla is a professor at Wake Forest Institute for Regenerative Medicine (WFIRM). Prior to joining WFIRM he played a key role in the nation's first approved hand transplant program at the University of Louisville before joining the University of Pittsburgh Medical Center, where his efforts were fundamental to the institutional approval, federal funding, and establishment of the nation's second upper extremity transplant program, with eight upper extremity transplants. He has been a primary investigator across diverse programs ranging from upper extremity transplantation and organ preservation to eye transplantation and novel graft-targeted drug delivery in vascularized composite allotransplantation.



Connie Rhee, M.D. – University of California, Irvine – Dr. Rhee is a board-certified UCI Health nephrologist who specializes in treating kidney diseases and kidney dialysis. Her clinical interests include diabetes-related kidney disease, endocrine disorders in kidney disease and thyroid dysfunction in chronic kidney disease. She earned her MD degree at Northwestern University's Feinberg School of Medicine in Chicago. She also completed a Master's of Science in epidemiology at Harvard University's School of Public Health. Her research interests include the study of endocrine derangements in chronic kidney disease and end-stage renal disease patients. She also studies racial disparities and nutrition in in chronic kidney disease and end-stage renal disease, as well as dialysis outcomes. She has received grants from the National Institutes of Health, the National Kidney Foundation and the American Thyroid Association, and has published more than 120 manuscripts.

Preethi Yerram, M.D. – University of Missouri – Dr. Yerram is a Nephrology Specialist in Columbia, MO and has over 19 years of experience in the medical field. She graduated from University of Health Science / Siddhartha Medical College in 2003. She is affiliated with medical facilities such as Ellis Fischel Cancer Center and Lake Regional Health System.

MISAA Business Proposition

The Problem

- Tacrolimus (Tac) is an essential immunosuppressive drug for solid-organ and tissue transplant patients
- Frequent patient monitoring is critical
- LC-MS/MS is time consuming, painful and contributes to patient non-compliance.

The Solution

- MISAA Tac-Assay eLFA has been validated against LC/MS-MS with 54 kidney transplant recipients to date
- Strong interrelationship – Pearson correlation r = 0.90
- Good agreement – Bland-Altman analysis mean bias = 0.7 ng/mL at 95% limit of agreement.

Current Status

- 510(k) FDA pre-market submission FDA - underway
- Discussions with Corporate Investors. 1 term sheet to license
- Seed round open to continue FDA process

The Offering

- Looking to raise $1MM
- Funding for FDA process and product development

Pains in the Existing Transplant Marketplace

- **Hospital systems' incentive to reduce costs** – "*…The pandemic has pushed the U.S. healthcare system to the brink, with an estimated $54 billion in net income losses for hospitals in 2021 alone…"* [American Hospital Association, "Data brief: Health care workforce challenges threaten hospitals' ability to care for patients" https://www.aha.org/fact-sheets/2021-11-01-data-brief-health-care-workforce-challenges-threaten-hospitals-ability-care]

- **Monitoring is complex and demanding** – "*… delivery of the results after a significant delay, and interpretation according to complex algorithms…*" [T. Buclin et al., "Monitoring drug therapy" Br J Clin Pharmacol 2012] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3391519/

- **Non-compliance** – "*…Recent literature reviews combining the results from over 300 articles estimated the prevalence of poor immunosuppression compliance among kidney transplant recipients to be between 22% and 28%..."* [B.W. Pinsky et.al., "Transplant outcomes & economic costs associated with patient noncompliance to immunosuppression" Am J Transplant 2009]

Patient Non-compliance to Protocols

- **Restrictive schedule** – "…tests are time sensitive; patients treated on a twice-daily basis have blood draws exactly 12 hours after their previous dose. The schedule's rigidity causes problems for both patients and healthcare providers... The most common practice for transplant centers is to check the tacrolimus trough concentration before a patient's morning dose of IR-Tac. This standardization of practice to accommodate laboratory work can result in many patients presenting for their blood draws at or around the same time, and can create logistical challenges for providers and patients alike." https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6032903/

- **Ease of access to testing** – "As of 2020, about 57 million Americans lived in a rural area, according to Statista. These individuals face a litany of challenges, ranging from where they live to having enough doctors to provide care…additionally, per AHA statistics, approximately 3.5 million patients go without care because they cannot access transportation to their providers." https://patientengagementhit.com/news/top-challenges-impacting-patient-access-to-healthcare

- **Cost of medication** – "The federal government will pay more than $100,000 to give someone a kidney transplant, but after three years … will often stop paying for the drugs needed to keep that transplanted kidney alive." https://www.npr.org/sections/health-shots/2016/12/22/506319553/medicare-pays-for-a-kidney-transplant-but-not-the-drugs-to-keep-it-viable