

**AddGraft**  
THERAPEUTICS



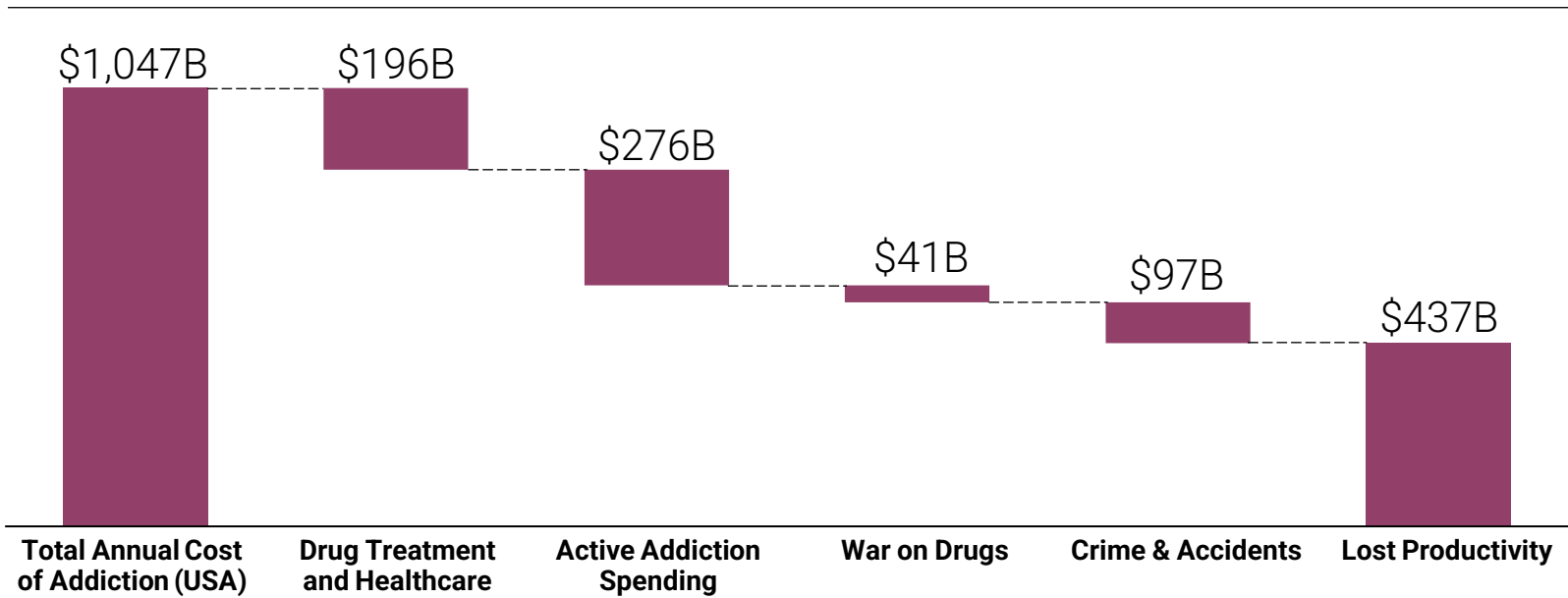
**Deploying cutting edge genetic  
treatments to address addiction**



# Scope of Addiction

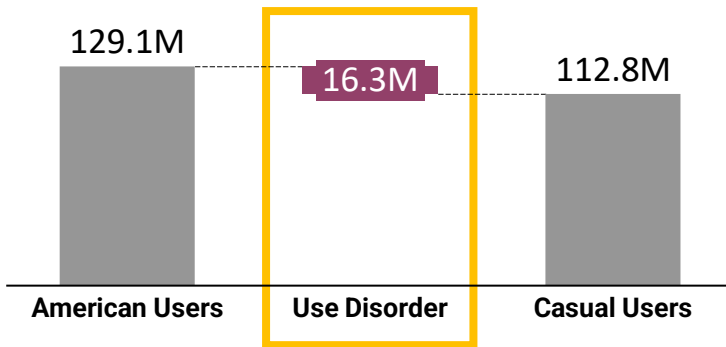
Addiction costs the USA **over \$1 trillion** every year

ANNUAL ADDICTION RELATED COST IN THE USA



Costs of addiction are equivalent to ~6% of US GDP or ~17% of all US government spending

# The Alcohol Problem



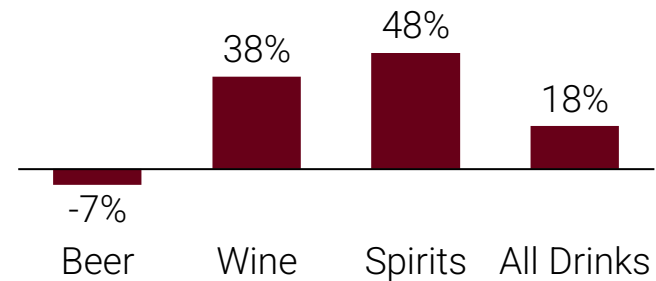
\$224B

**Total Cost USA**  
(Annually)

88k+

**American Lives Lost**  
(Annually)

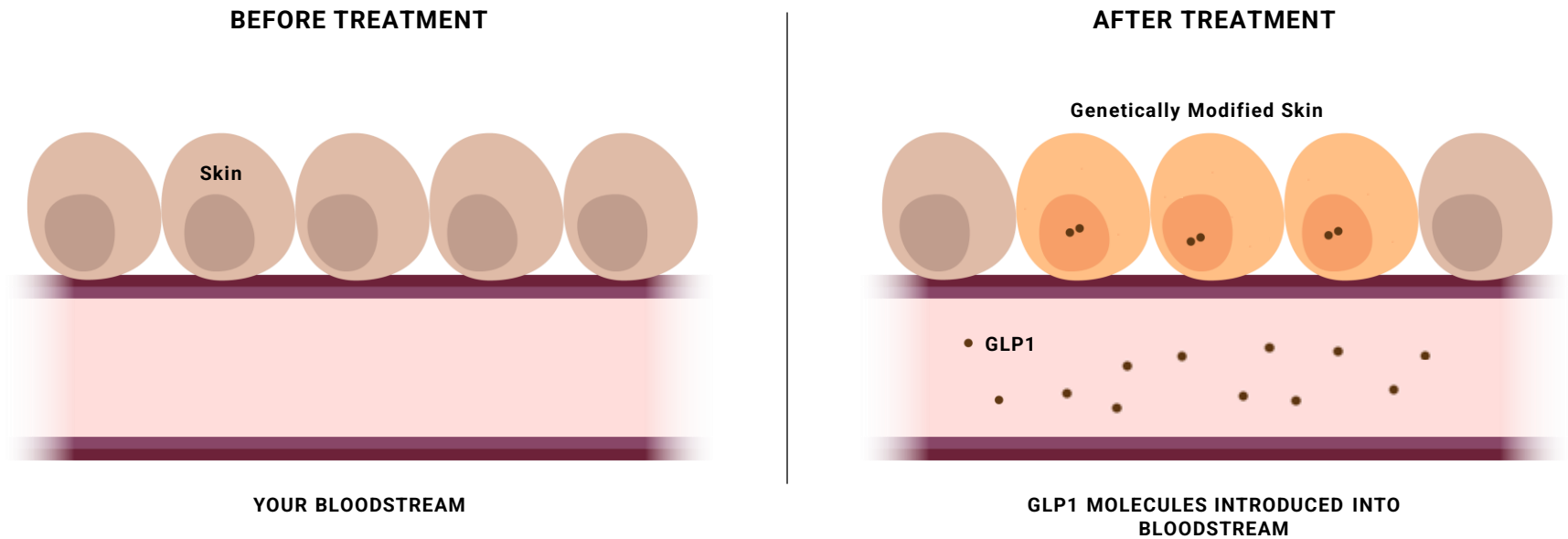
**USA Per Capita Consumption Change**  
(1998 to 2018)



Alcohol abuse disorder (AUD) currently see's 3 in 4 patients treated failing to preserve their sobriety within the first year of treatment

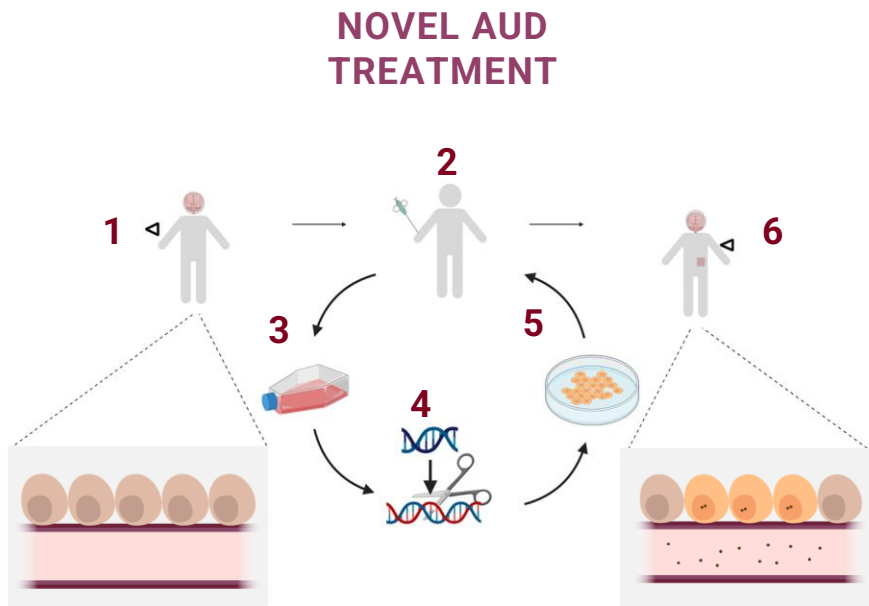
# Our Technology

AddGraft Therapeutics' unique treatment for AUD **deploys directly in the bloodstream**



AddGraft Therapeutics' unique treatment utilizes a skin bioengine to deploy natural occurring molecules to treat addiction

# Our Technology



## PROCEDURE

1. Individual with AUD
2. AUD patient has sample of skin taken (fingernail size)
3. Skin is quickly relocated to laboratory partner
4. Skin is edited using stem cell and CRISPR technologies
5. Skin sample is cultured and grown for 3-week period
6. Modified skin is implanted back into original patient as a skin graft

## FOLLOW ON

- Patient has limited cravings for alcohol and limited desire to drink in case of relapse
- Patient utilizes common antibiotics to “activate” skin graft in future case of cravings
- Patient utilizes cognitive behavioral treatment for 12 weeks with behavioral experts

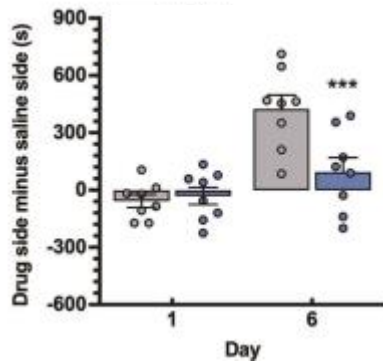
AddGraft Therapeutics' unique treatment is implemented through a one time, minimally invasive surgery

# Our Technology

Our treatment has shown highly encouraging preclinical results and **successfully prevents alcohol addiction, relapse and reducing active drinking**

## PREVENTING ADDICTION

**Experiment:** Testing addiction rates in grafted and non grafted mice

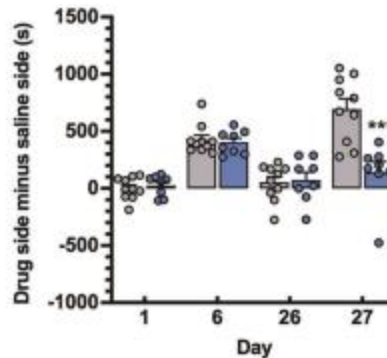


- Not Grafted Mice
- Grafted Mice

**Results:** Addictive behavior not developed in grafted mice

## PREVENTING RELAPSE

**Experiment:** Testing relapse rates in grafted versus non grafted mice

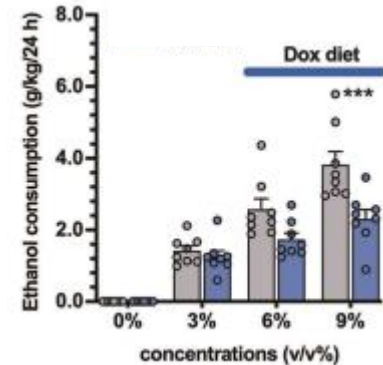


- Not Grafted Mice
- Grafted Mice

**Results:** Formerly addicted mice when grafted did not relapse

## REDUCING ACTIVE DRINKING

**Experiment:** Testing alcohol consumption rates in grafted and non grafted mice



- Not Grafted Mice
- Grafted Mice

**Results:** Grafted mice showed reduced ongoing drinking levels

# Key Features

## TREATING CO-ABUSE



Single treatment for alcohol, nicotine, cocaine and **co-abuse**



Platform coverage **prevents secondary abuse** development

## INTELLECTUAL PROPERTY



**Patent filed** and pending – USA, China and Europe



3 publications and 2 peer reviews corroborating preclinical results

## TECHNOLOGY FEATURES



Long lasting, highly effective and minimally invasive



Autograft minimizes immune response



Treatment is highly successful in mouse models

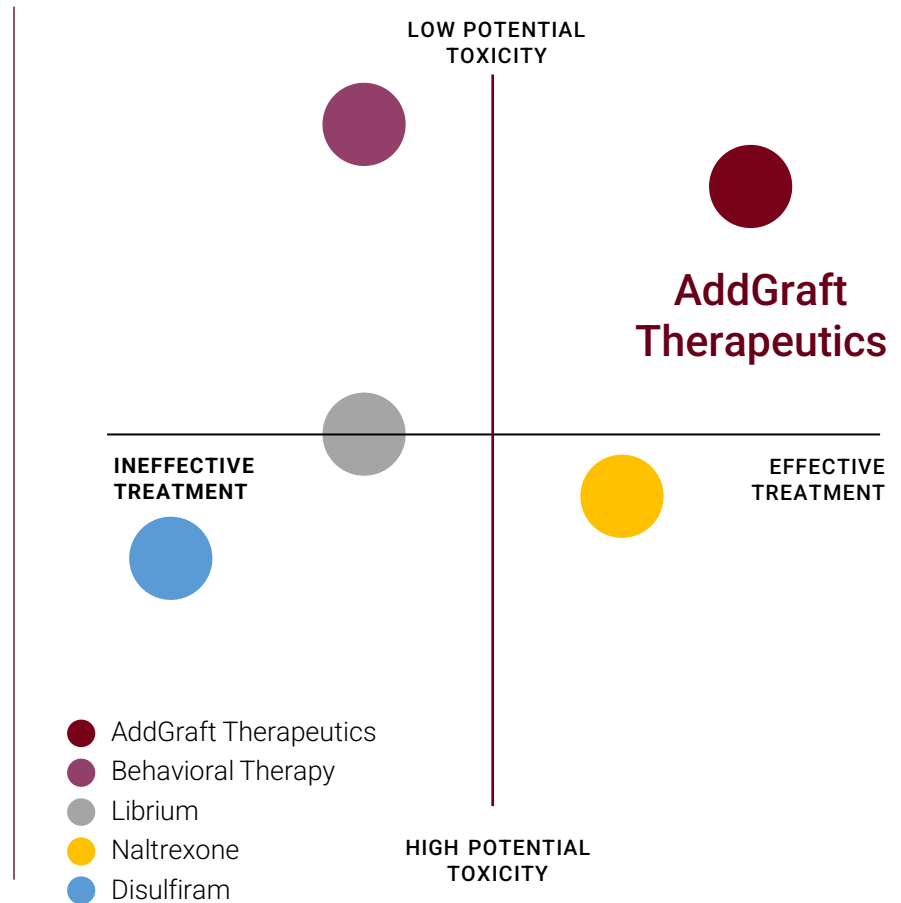


Bioengine stably supplies GLP1 molecule to bloodstream

AddGraft's onetime treatment provides lifelong and diverse benefits to patients along with unique market and technological advantages

# Market Assessment

Current AUD treatments, approved by the FDA, **have potential for severe health complications and efficacy issues**





# Market Assessment

ESTIMATED TREATMENT PRICE <b>\$60k cost to treat</b>	PRIMARY/ENTRANCE MARKET <b>Alcohol</b>	SECONDARY MARKET <b>Nicotine</b>	TERTIARY MARKET <b>Cocaine</b>
MARKET ENTRANCE	FDA APPROVAL	SECONDARY FDA APPROVAL	TERTIARY FDA APPROVAL
<b>Total Addressable Market</b>	\$982B 16.3M with use disorder	\$2,012B 33.4M with use disorder	\$61B 1M with use disorder
<b>Service Addressable Market</b>	\$90B 9% use treatment	\$624B 31% use treatment	\$12B 20% use treatment
<b>Service Obtainable Market</b>	<b>\$5B - \$29B</b> 5-20% captured	<b>\$12B - \$62B</b> 2-10% captured	<b>\$1.5B - \$2.5B</b> 25% employed 50-80% captured

AddGraft's single surgery, with no alteration of chemical or mechanical deployment, treats alcohol, nicotine, cocaine and co-abuse

# Market Entrance

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AddGraft will initially seek to treat AUD patients in the state of Illinois, through partnerships with hospitals, who are currently routing patients to expensive rehabilitation facilities

## CURRENT STATE

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- **Patients Use:** Stays at behavioral rehab facilities with inclusion of MAT
- **Cost Per Treatment:** \$5k - \$50k+ (often requires multiple treatments)
- **Acquired Through:** Post hospital visit reroute, drug court assignment or personal outreach
- **Paid By:** Portion of insurance, government funding and out of pocket expense
- **Expectations:** Relapse at ~75%

## ADDGRAFT ENTRANCE

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- **Patients Use:** AddGraft's one time treatment
- **Cost Per Treatment:** \$60k
- **Acquired Through:** Post hospital visit reroute and behavioral partnerships
- **Paid By:** Portion of insurance, government funding and out of pocket expense
- **Expectations:** Rate of relapse to be significantly lower (exacts to be determined in human trials phase 2)

# Team

## Management Team



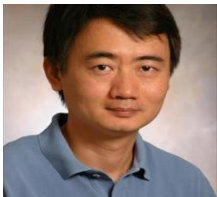
**Ryan Meyers**  
Chief Executive Officer

MBA Candidate at University of Chicago Booth,  
Venture Capital, Healthcare Management  
Consulting



**Dr. Ming Xu**  
Chief Science Officer

Professor, University of Chicago – Neurobiology,  
Addiction Specialist



**Dr. Xiaoyang Wu**  
Chief Technology Officer

Associate Professor, University of Chicago – Tissue  
Engineering, Regenerative Medicine, Platform Inventor

## Advisory Board



**Michael Darcy**  
Former CEO of Gateway Foundation

Michael spent 30 years as the CEO and President of the  
Gateway Foundation, Illinois's largest substance abuse  
treatment provider



**Dimitra Georganopoulou, PhD**  
C-Suite Biotech Executive

Dimitra has spent decades in biotech with experiences from  
Chief Business Officer of myGenomeRx to directing innovation  
at top level institutions like Northwestern and MIT

## Investors

Limitless Ventures



**C.B.A.N.**

Chicago Booth Angel Network

# Partners and Programs

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## Affiliations and Awards

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Addiction Medicine.  
Saving Lives.



## Current Incubator/Program Participation

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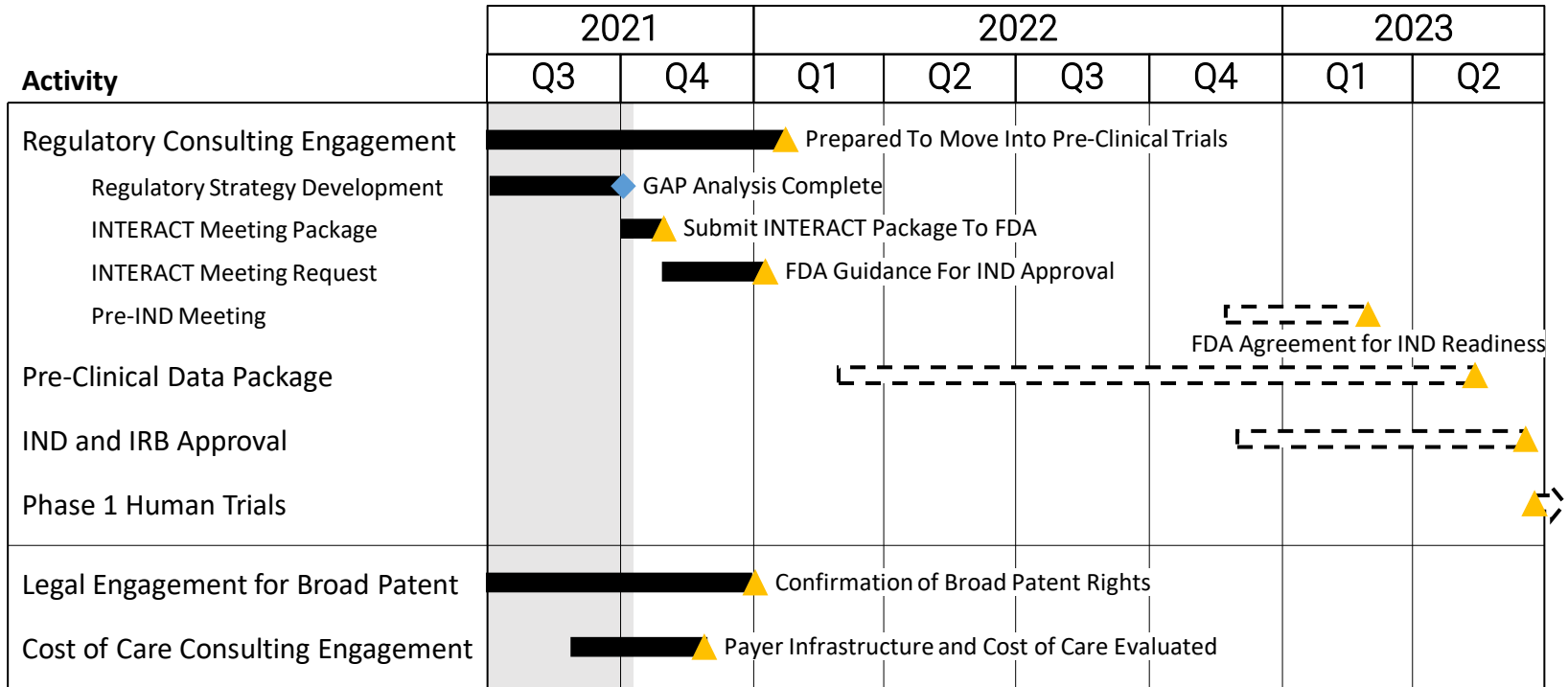
## Completed Programs

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# Critical Next Steps

In the immediate future, establishing a clear path to phase 1 IND approval with the FDA for our revolutionary new technology **will create significant value**



▲ Represents Value Creation Point

◆ Represents Completed Value Creation Point



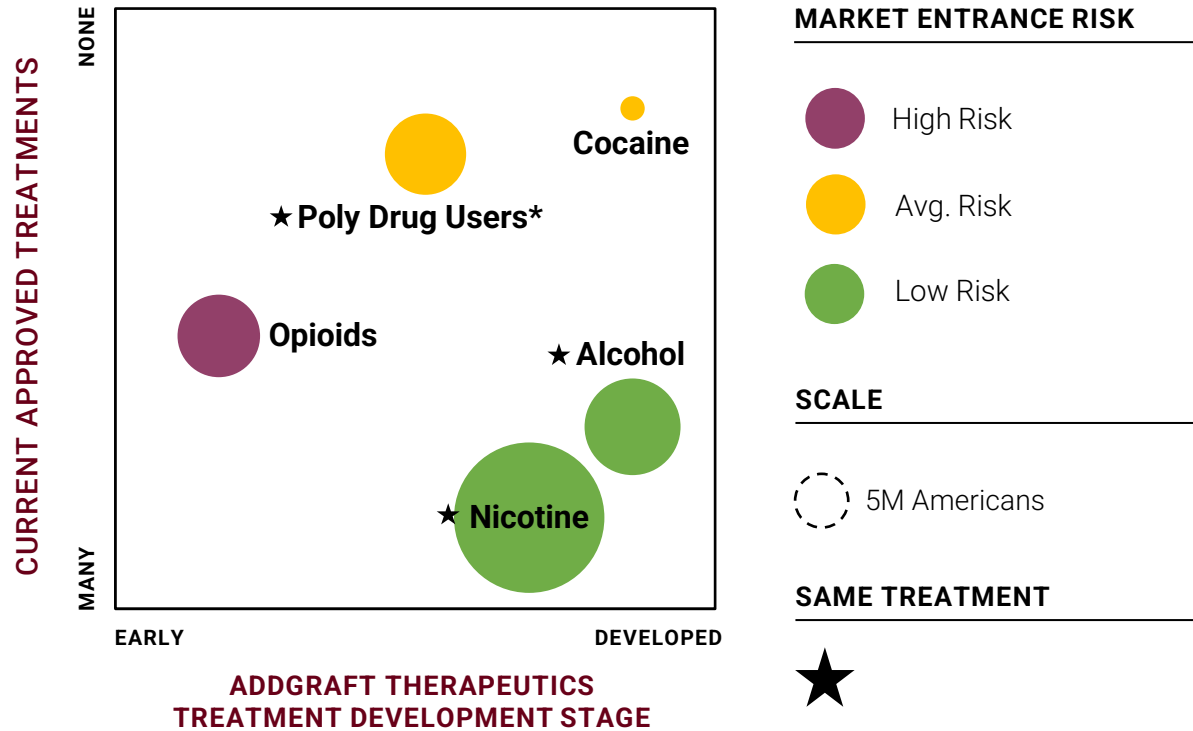
# Fundraising

	VALUE	TIMING	SIGNIFICANT MILESTONES
<b>Previous Funding</b>	\$3.1M in NIH Grants	2016 – January 2021	<ul style="list-style-type: none"><li>• Technology successfully developed and tested in mouse models</li></ul>
<b>Pre-Seed</b>	\$110k	July 2021 – January 2022	<ul style="list-style-type: none"><li>• FDA confirmation of preclinical and clinical approach</li><li>• Legal confirmation of Broad patent rights</li><li>• Payer infrastructure confirmed</li></ul>
<b>Seed</b>	\$5.8M (Projected)	January 2022	<ul style="list-style-type: none"><li>• Conduct preclinical trials scoped and confirmed by the FDA (Tox, CMC, PK, Etc.)</li><li>• Receive IND approval</li></ul>

AddGraft has successfully raised \$110k in our pre-seed round to fund final aspect of our FDA approved planning

# Opportunity Summary

## MARKET ENTRANCE ANALYSIS



Our beachhead market will be for AUD patients, but this platform technology can service many other addictions/disorders

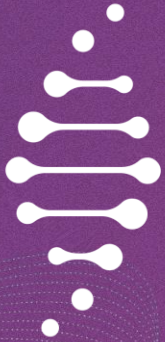
# Opportunity Summary

## MARKET ENTRANCE ANALYSIS

Use Disorder	Discovery	Proof of Concept	FDA Engagement	IND Enabling Studies	Phase 1
Alcohol	[Progress bar spanning Discovery, Proof of Concept, and FDA Engagement]				
Nicotine	[Progress bar spanning Discovery and Proof of Concept]				
Cocaine	[Progress bar spanning Discovery and Proof of Concept]				
Opioids	[Progress bar spanning Discovery]				
<b>Additional Indications</b>					
Cognitive Decline	[Progress bar spanning Discovery]				
Diabetes	[Progress bar spanning Discovery]				
Other	[Progress bar spanning Discovery]				

Our beachhead market will be for AUD patients, but this platform technology can service many other addictions/disorders





# AddGraft

THERAPEUTICS



Let's continue  
the conversation!

**Ryan Meyers**

CEO

[Ryan@addgrafttherapeutics.com](mailto:Ryan@addgrafttherapeutics.com)

(248) 770 - 8438



The background features a dark purple gradient with several overlapping, wavy, semi-transparent bands in shades of purple and green. These bands create a sense of depth and movement. In the center, the word "Appendix" is written in a clean, white, sans-serif font.

# Appendix



# Market Assessment – Alcohol Abuse Treatment

Within the alcohol abuse treatment market, there are 3 FDA approved treatments which are expensive over a patient’s lifetime, produce significant negative side effects and have high rates of relapse



**Behavioral Therapy**



**Chlordiazepoxide**



**Acamprosate**



**Disulfiram**



**Skin Graft Gene Therapy**

	Behavioral Therapy	Chlordiazepoxide	Acamprosate	Disulfiram	Skin Graft Gene Therapy
Frequency	30-90 days	Multiple Times Daily	Multiple Times Daily	Daily	Daily
Stage	Available (50-80% relapse rate year one)	FDA Approved	FDA Approved (40% - 60% relapse rate)	FDA Approved (80% relapse rate)	Multiple years from FDA approval
Ease for Patient	—	—	—	...	+
Complication / Toxicity	+	—	—	—	+
Cost	\$30k/visit	50 - 60k/year	1.5k/year	<1k per year	\$60k, one-time

# Technology Advantages Between Substances

	Cocaine	Alcohol	Nicotine	Opioids	Co-abuse
Reducing Use	+	+	+	?	...
Preventing Addiction	+	+	+	+	+
Preventing Relapse	+	+	+	+	+
Technology Developed	+	+	+	-	+
Preventing Overdose Death	+	-	-	?	...

AddGraft's treatment is extremely effective at treating various aspects of addictive behavior

# Team Details

Name	Employment Type	Position	Qualifications	Responsibilities
Ryan Meyers	Full Time	CEO	<ul style="list-style-type: none"> <li>Venture Experience – Evaluated deal flow, assisted portfolio companies, sourced deals</li> <li>Management Healthcare Consultant – Led clients through mergers, acquisitions and org change</li> <li>MBA Candidate Chicago Booth</li> </ul>	<ul style="list-style-type: none"> <li>Lead AddGraft’s strategy and general direction to commercialization</li> <li>Lead fundraising efforts and associated relations</li> <li>Maintain and manage business operations</li> <li>Execute financial plan and management</li> <li>Manage AddGraft’s team including hiring and external contractor decisions</li> <li>Complete additional tasks as required</li> </ul>
TBD	Full Time	CRO	<ul style="list-style-type: none"> <li>Experience PMO in regulatory processes and preclinical trials</li> <li>PHD or associated scientific degree from top university</li> </ul>	<ul style="list-style-type: none"> <li>Oversee preclinical and clinical study development, execution and regulatory strategy</li> <li>Supervise and manage associated regulatory contractors</li> <li>Own FDA relationship for AddGraft</li> <li>Act as PI when necessary/appropriate</li> </ul>
Dr. Ming Xu	Part Time	CSO	<ul style="list-style-type: none"> <li>Professor, University of Chicago – Neurobiology,</li> <li>25 years of studying addiction and considered addiction specialist</li> <li>PHD</li> <li>Over 100 career publications</li> </ul>	<ul style="list-style-type: none"> <li>Lead ownership of the scientific platform and deployment of technology</li> <li>Develop and collaborate to produce preclinical and clinical trial materials, procedures and required data</li> </ul>
Dr. Xiaoyang Wu	Part Time	CTO	<ul style="list-style-type: none"> <li>Associate Professor, University of Chicago – Tissue Engineering, Regenerative Medicine</li> <li>Skin based platform inventor</li> <li>PHD</li> </ul>	<ul style="list-style-type: none"> <li>Develop and collaborate to produce preclinical and clinical trial materials, procedures and required data</li> <li>Own skin graft development and technology expansion</li> </ul>

# Pre-Seed and Seed Budget

(\$ in 1,000s)

Item	Pre-Seed	Seed
<b>R&amp;D Costs</b>		
Phase 1 Pre Clinical Trials		5,000
<b>R&amp;D Subtotal</b>	<b>\$ -</b>	<b>\$ 5,000</b>
<b>Regulatory Consulting Subtotal</b>		
Regulatory Strategic Development	\$ 15	
INTERACT Meeting Services	42	
Pre-IND Meeting		140
IND Submission		200
<b>Regulatory Consulting Subtotal</b>	<b>\$ 57</b>	<b>\$ 340</b>
<b>Business Needs</b>		
AddGraft Team and Infrastructure	\$ 10	\$ 240
Additional Legal and Consulting Needs	18	100
PHI Utilizing Cost Of Care Engagement	15	
IP	10	200
<b>Business Needs Subtotal</b>	<b>\$ 53</b>	<b>\$ 540</b>
<b>Total Seed in SAFE's</b>	<b>\$ 110</b>	<b>\$ 5,880</b>

# Phase 1 Budget

Executing 10 surgeries in our phase 1 clinical trials is projected to cost \$617k

Phase 1 Trial Cost Input	2021 Cost
Surgeries (Per Patient)	\$ 37,000
Graft Manufacturing (Per Graft)	14,000
Administrative Costs (Per Patient)	6,000
<b>Treatment Total Per Patient</b>	<b>57,000</b>
<b>Treatment for 10 Patients</b>	<b>\$ 570,000</b>
Treatment Staff Compensation	\$ 47,000
<b>Total for 10 Patient Study</b>	<b>\$ 617,000</b>

Treatment	Per Patient Cost
Surgery 1: Skin Removal	
<i>Operation</i>	\$ 10,000
<i>Wound Closure</i>	500
<i>Dressings</i>	500
<i>Inpatient Dressings</i>	1,000
<b>Surgery 1: Skin Removal</b>	<b>\$ 12,000</b>
Surgery 2: Graft Installment	
<i>Operation</i>	\$ 15,000
<i>Wound Closure</i>	500
<i>Dressings</i>	500
<i>Inpatient Dressings</i>	1,000
<b>Surgery 2: Graft Installment</b>	<b>\$ 17,000</b>
Post Patient Follow Up (12 total)	\$ 6,000
Wound Care	2,000
<b>Treatment total</b>	<b>\$ 37,000</b>

Graft Manufacturing	Cost
Personnel	\$ 60,000
Supplies (per graft 6k across 10 patients)	60,000
Lab Use Hours (Projected 130 hours at 150/hour)	20,000
<b>Graft total for 10 patients</b>	<b>\$ 140,000</b>
<b>Per Patient Graft Cost</b>	<b>\$ 14,000</b>



# Projected Cost Scaling

Executing 10 surgeries in our phase 1 clinical trials is projected to cost \$617k

Surgeries	Per Patient Cost		
	Phase 1	Phase 2	Phase 3 / Commercial
<b>Surgery 1: Skin Removal</b>			
Operation	\$ 10,000	\$ 9,000	\$ 7,000
Wound Closure	500	500	400
Dressings	500	500	400
Inpatient Dressings	1,000	1,000	800
<b>Surgery 1: Skin Removal</b>	<b>\$ 12,000</b>	<b>\$ 11,000</b>	<b>\$ 8,600</b>
<b>Surgery 2: Graft Installment</b>			
Operation	\$ 15,000	\$ 14,000	\$ 12,000
Wound Closure	500	500	400
Dressings	500	500	400
Inpatient Dressings	1,000	1,000	800
<b>Surgery 2: Graft Installment</b>	<b>\$ 17,000</b>	<b>\$ 16,000</b>	<b>\$ 13,600</b>
Post Patient Follow Up (12 total)	\$ 6,000	\$ 6,000	\$ 3,000
Wound Care	2,000	2,000	1,500
<b>Surgeries Total</b>	<b>\$ 37,000</b>	<b>\$ 35,000</b>	<b>\$ 26,700</b>
<b>Graft Manufacturing</b>			
Personnel (60k total \$10/patient)	\$ 6,000	\$ -	\$ -
Supplies (per graft \$6k across 10 patients)	6,000	6,000	5000
Lab Use Hours (Projected 130 hours at \$150/hour)	2,000	3,250	3000
<b>Per Patient Graft Cost</b>	<b>\$ 14,000</b>	<b>\$ 9,250</b>	<b>\$ 8,000</b>
<b>Treatment Total Per Patient</b>	<b>\$ 51,000</b>	<b>\$ 44,250</b>	<b>\$ 34,700</b>
<b>Estimated Price For Patients</b>			<b>\$ 60,000</b>
<b>Gross Margin</b>			<b>\$ 25,300</b>
<b>Gross Margin %</b>			<b>42%</b>

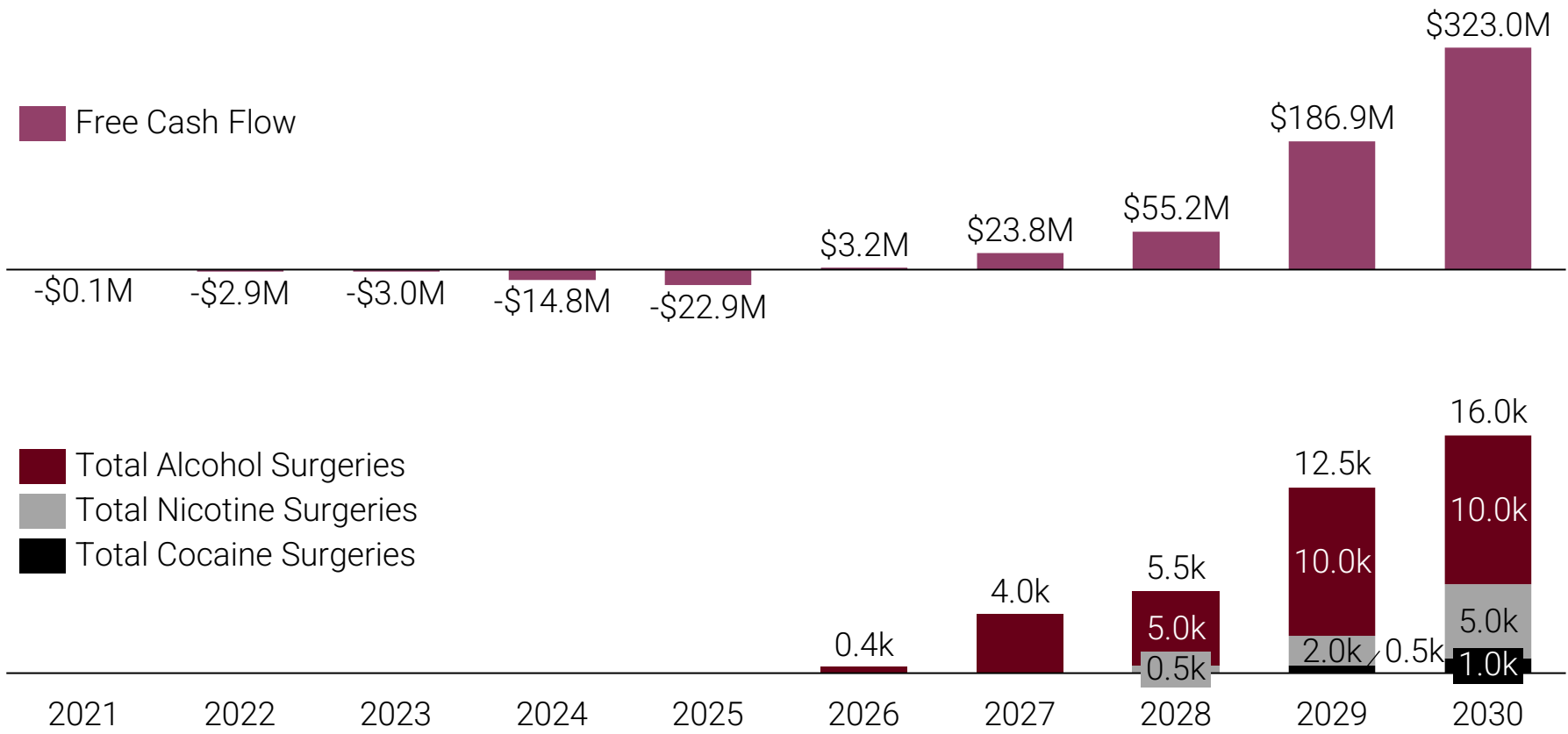
# Financial Projections

Current projections put AddGraft prepared to begin generating revenue and attaining positive cash flows in 2026 with FDA approval for treating AUD

(\$ in 000s)	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030
<b>Total Revenue</b>	\$ -	\$ -	\$ -	\$ -	\$ -	\$ 40,000	\$ 240,000	\$ 350,000	\$ 770,000	\$ 1,090,000
COGS - Direct Material	-	-	-	-	-	13,880	138,800	190,850	433,750	607,250
COGS - Direct Labor	-	-	-	-	-	1,000	1,350	3,375	7,088	8,505
<b>Cost of Goods Sold</b>	-	-	-	-	-	<b>14,880</b>	<b>140,150</b>	<b>194,225</b>	<b>440,838</b>	<b>615,755</b>
<b>Gross Profit</b>	-	-	-	-	-	<b>25,120</b>	<b>99,850</b>	<b>155,775</b>	<b>329,163</b>	<b>474,245</b>
<i>% of Revenue</i>	0%	0%	0%	0%	0%	63%	42%	45%	43%	44%
Pre-Clinical Direct Materials	-	2,567	2,550	-	500	1,033	5,117	-	-	-
Pre-Clinical Direct Labor	-	140	230	-	100	125	140	-	-	-
Clinical Direct Material	-	-	-	1,029	2,983	1,029	4,012	4,012	2,983	-
Clinical Direct Labor	-	-	-	230	409	230	639	639	409	315
Clinical Trial Study Expense	-	-	-	2,978	10,450	2,978	13,428	13,428	10,450	-
<b>Total R&amp;D Expense</b>	-	<b>2,707</b>	<b>2,780</b>	<b>4,237</b>	<b>14,442</b>	<b>5,395</b>	<b>23,336</b>	<b>18,079</b>	<b>13,842</b>	<b>315</b>
<b>Total SG&amp;A</b>	<b>90</b>	<b>248</b>	<b>250</b>	<b>2,523</b>	<b>4,415</b>	<b>15,453</b>	<b>46,360</b>	<b>60,268</b>	<b>72,322</b>	<b>65,090</b>
<b>EBITDA</b>	<b>(90)</b>	<b>(2,955)</b>	<b>(3,030)</b>	<b>(6,760)</b>	<b>(18,858)</b>	<b>4,271</b>	<b>30,154</b>	<b>77,427</b>	<b>242,998</b>	<b>408,840</b>
<i>% of Revenue</i>	0%	0%	0%	0%	0%	11%	13%	22%	32%	38%
Depreciation	-	2	6	8	8	248	220	56	91	295
<b>Operating Profit</b>	<b>(90)</b>	<b>(2,957)</b>	<b>(3,036)</b>	<b>(6,768)</b>	<b>(18,866)</b>	<b>4,023</b>	<b>29,934</b>	<b>77,372</b>	<b>242,907</b>	<b>408,545</b>
<i>% Margin</i>	0%	0%	0%	0%	0%	10%	12%	22%	32%	37%
Taxes	-	-	-	-	-	845	6,286	16,248	51,011	85,794
<b>Net Income</b>	<b>(90)</b>	<b>(2,957)</b>	<b>(3,036)</b>	<b>(6,768)</b>	<b>(18,866)</b>	<b>3,178</b>	<b>23,648</b>	<b>61,124</b>	<b>191,897</b>	<b>322,751</b>
(+) Depreciation	-	2	6	8	8	248	220	56	91	295
(-) Capex	10	20	10	8,080	4,055	100	25	6,021	5,052	25
<b>Free Cash Flow</b>	<b>\$ (100)</b>	<b>\$ (2,975)</b>	<b>\$ (3,040)</b>	<b>\$ (14,840)</b>	<b>\$ (22,913)</b>	<b>\$ 3,326</b>	<b>\$ 23,843</b>	<b>\$ 55,158</b>	<b>\$ 186,936</b>	<b>\$ 323,021</b>
<i>% Margin</i>	0%	0%	0%	0%	0%	8%	10%	16%	24%	30%

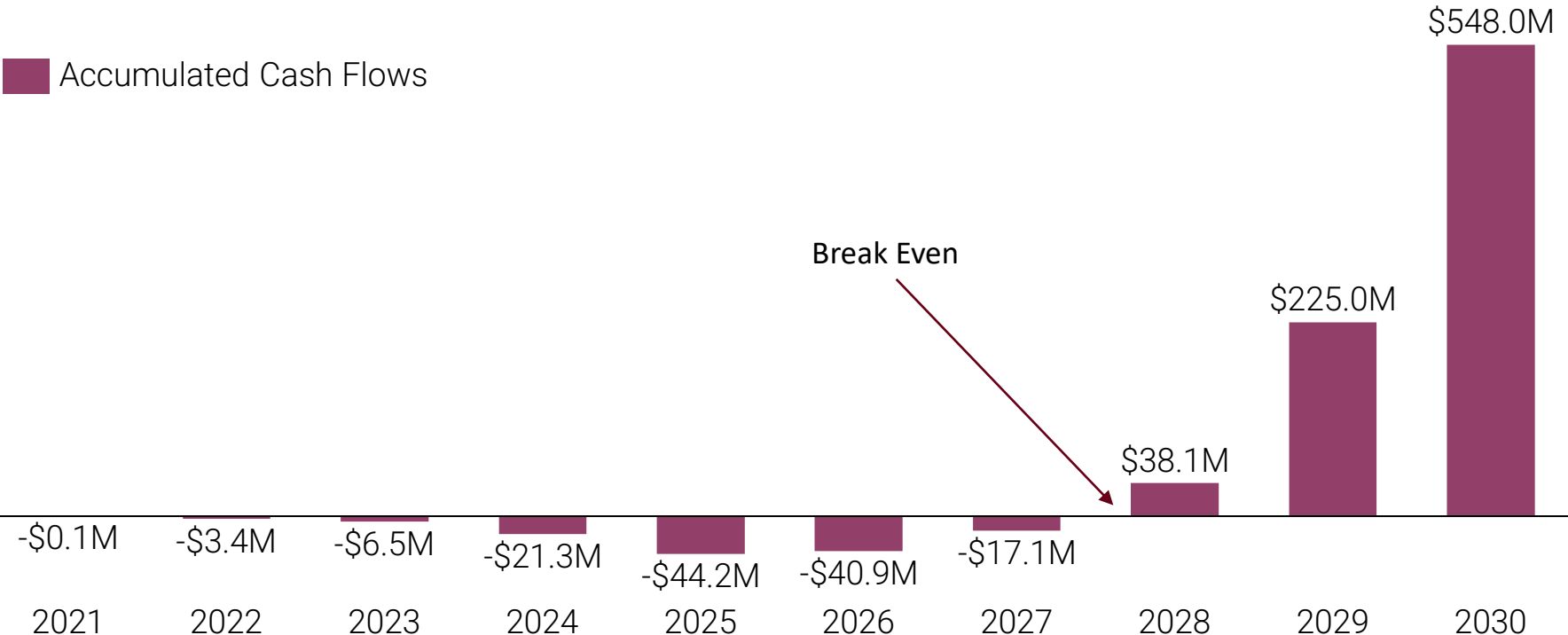
# Financial Projections – FCF

Current projections put AddGraft prepared to begin generating revenue and attaining positive cash flows in 2026 with FDA approval for treating AUD



# Financial Projections – Break Even

Current projections puts AddGraft prepared to reach a break even point conservatively in 2028 (roughly 7k total surgeries completed)

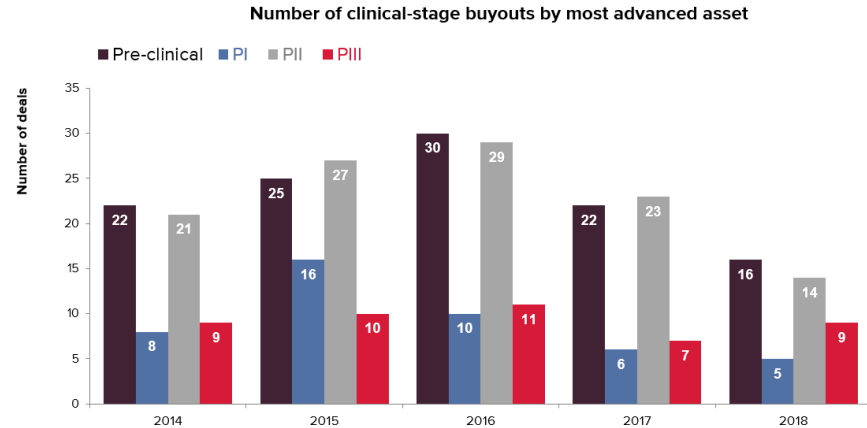


# Opportunity Summary

Our venture has multiple potential endpoints from an early exit to full scaling and development of our platform

## Pre FDA-Approval Exit

Exit opportunities range based on development stage and results of trials



## Post FDA Scaling

Opportunity, after FDA approval, to develop business offerings and multiple addiction markets

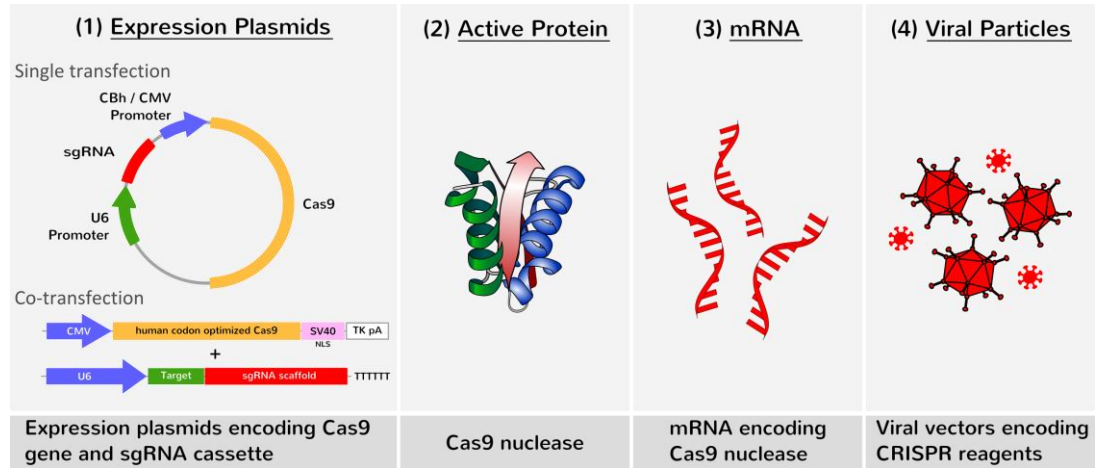
- Opioids
- Cocaine
- Nicotine
- Poly Drug Use



# CRISPR Summary

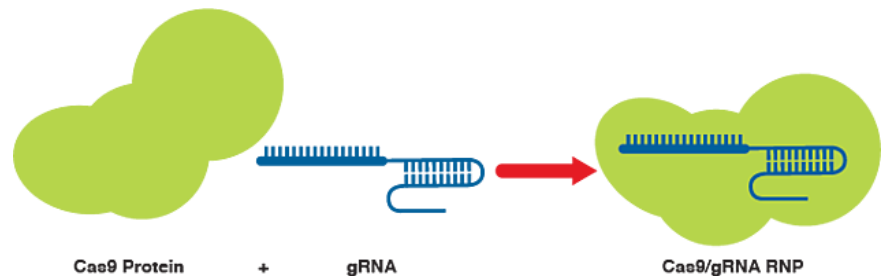
## Current State

Utilizing a DNA based approach to deliver Cas9 protein, gRNA and a targeting vector for genome editing



## Future State

Directly utilize Cas9 RNP complex (commercially available) to perform genome editing



AddGraft's future process for applying CRISPR will be simplified through the use of commercially available Cas9 RNP

# Clinical Success Rate

AddGraft's unique gene therapy and CAR T similar treatment has a higher likelihood of approval than other therapies in development

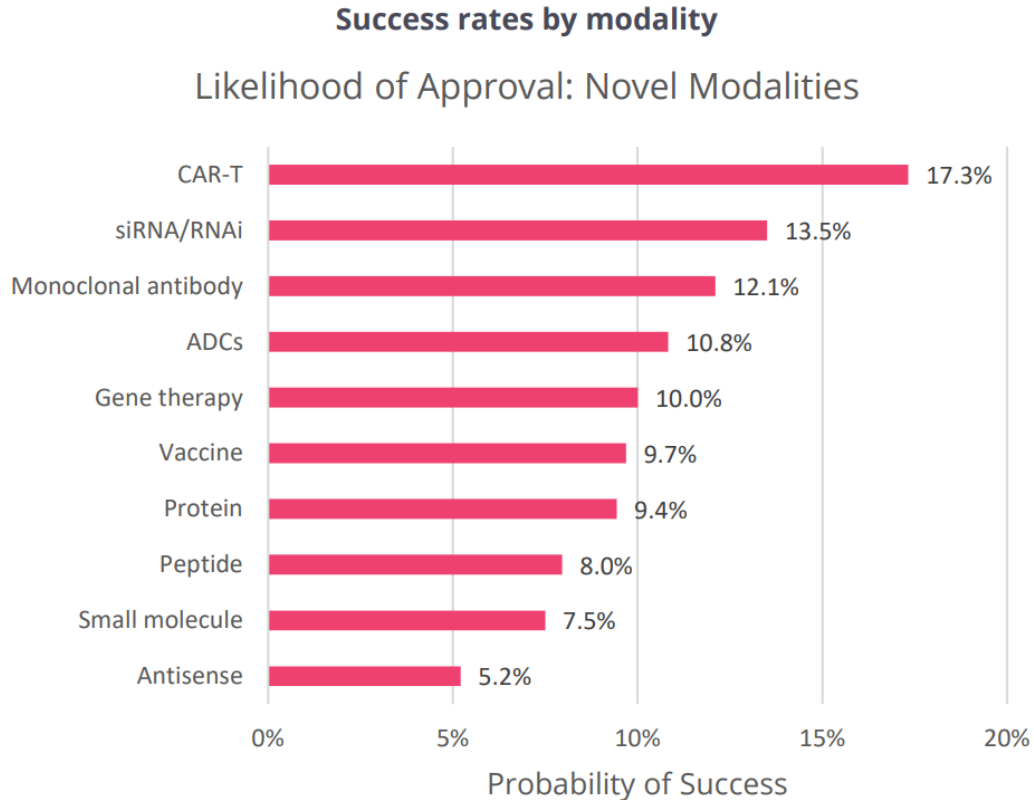


Figure 10a: LOA from Phase I for drugs based on modality. Chart of LOA from Phase I, displayed highest to lowest by drug modality.

# Our Technology

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Molecular  
Psychiatry

 CellPress





2 Peer Reviews

- *“the development of an ex vivo platform that can combine both precise genome editing in vitro with effective application of engineered cells in vivo will provide significant benefits for the treatment of many human diseases”*
  - - Cell Press (8/3/2017)
- *“The exciting potential of Xu [and Wu] and colleagues’ approach for treating cocaine dependence in afflicted individuals calls for studies that address these questions.”* - Nature Biomedical Engineering (2/3/2019)

# Doxycycline Safety

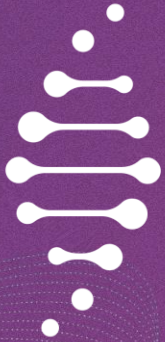
Doxycycline is commonly prescribed for multiple months to treat various afflictions including 4-month prescriptions to fight acne

Institution / Source	Disease/Affliction	Prescription length
	Acne	3-4 months
	Chronic Obstructive Pulmonary Disease (COPD)	"Long Term"

## Key Insight:

Due to the nature of addiction a 90-day period is enough time for extinction of the addiction. AddGraft's treatment can be successful in utilizing Doxycycline in windows shorter than current use for less significant disease.





# AddGraft

THERAPEUTICS



## Cocaine Specifics



# Worldwide Problem

Despite a ~64% relapse rate and \$21B lost per year in the USA by cocaine usage, there are no current market approved drugs to treat abuse

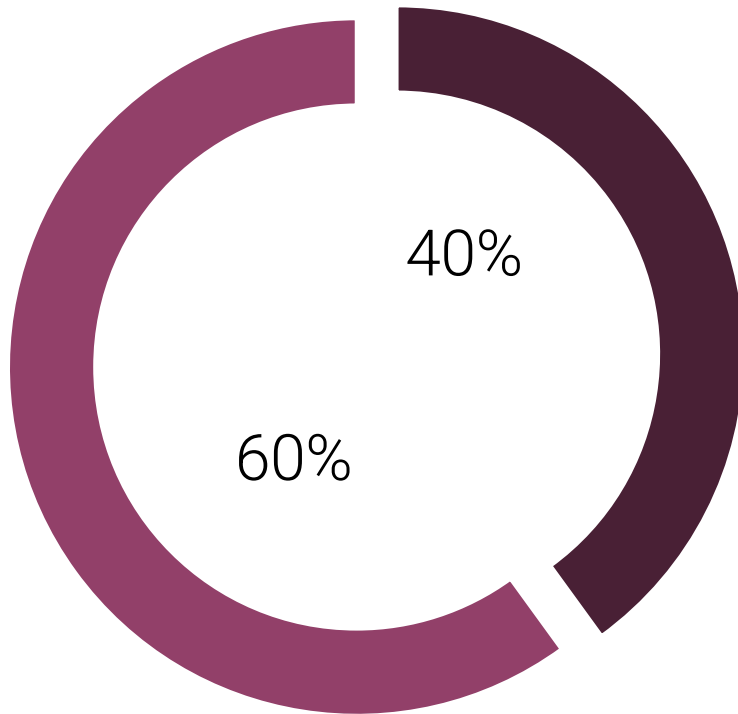
Cocaine Statistics	USA	Worldwide
Users	5M	19M
Addicts/Abusers	1M	11.6M*
ER Visits (Annual)	505k	
Primary Treatment	Behavior Intervention	Behavior Intervention
Approved Drugs	0	0
Usage Trends	Stable	Growing

\*Represents an assumption that addict percentage worldwide is similar to that of the USA at 60%

# Co-Abuse Problem

60% of cocaine abusers also abuse alcohol, causing the likelihood of death to increase to 20x greater than the use of either individually

## 1M Cocaine Abusers in the USA



## Alcohol Abuse Disorder In The USA

**50+%**

Relapse Rate

**14.1M**

PEOPLE

**\$281B**

Lost Annually

**3** Approved

Medications

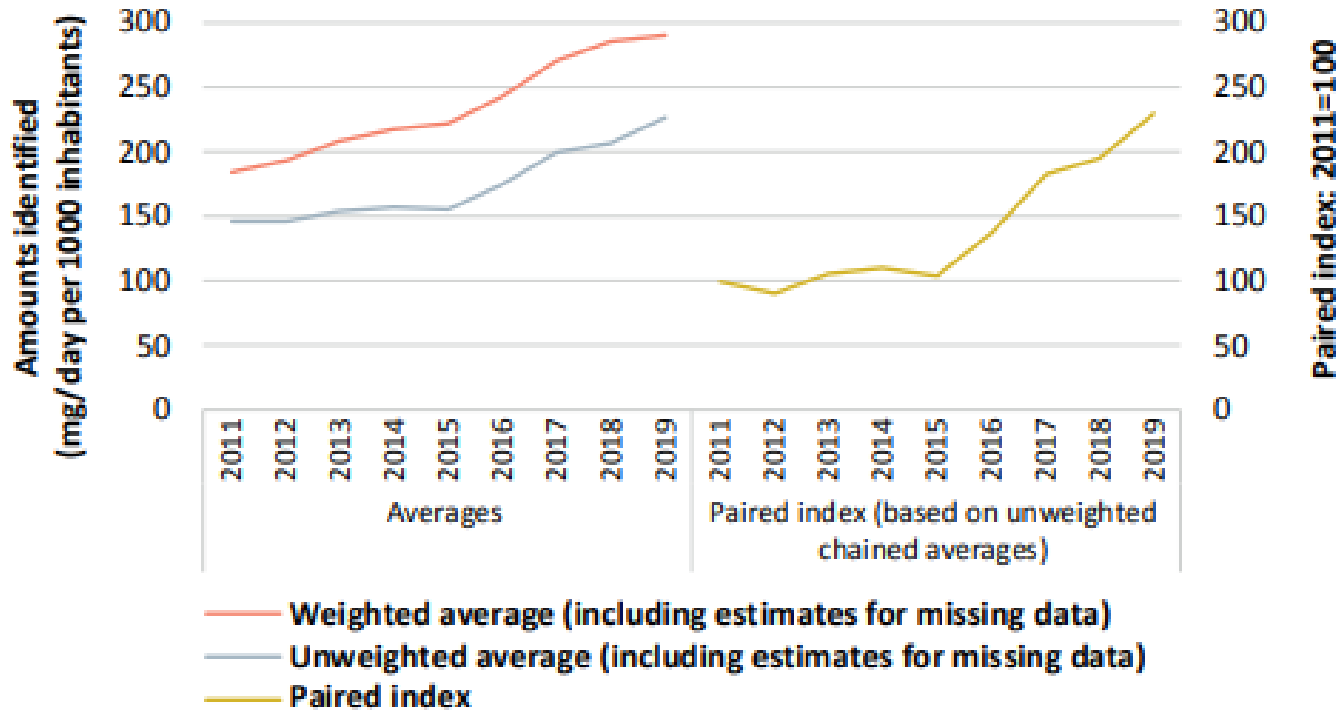
- Cocaine Without Alcohol
  - 405k
- Cocaine With Alcohol
  - 606k



# Problem

Europe has seen nearly 50% cocaine usage increase since 2011

**FIG. 27** Benzoylcegonine (cocaine metabolite) found in wastewater, 136 cities in Europe, 2011–2019

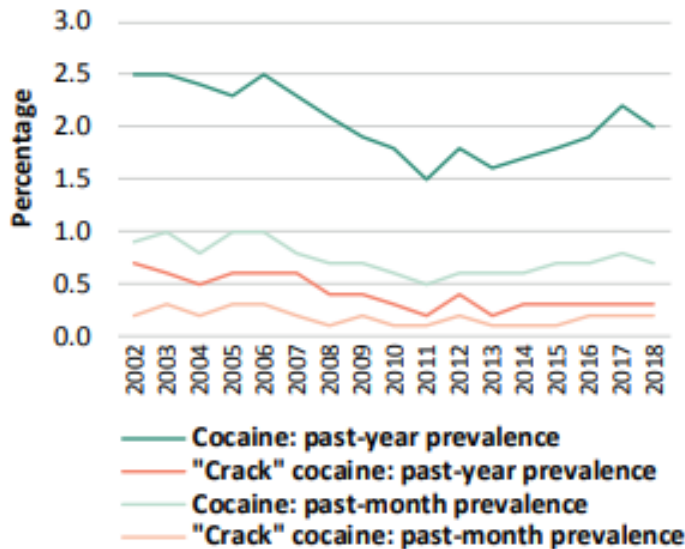


Source: UNODC calculations based on wastewater data provided by Sewage Analysis CORE group Europe (SCORE).

# Problem

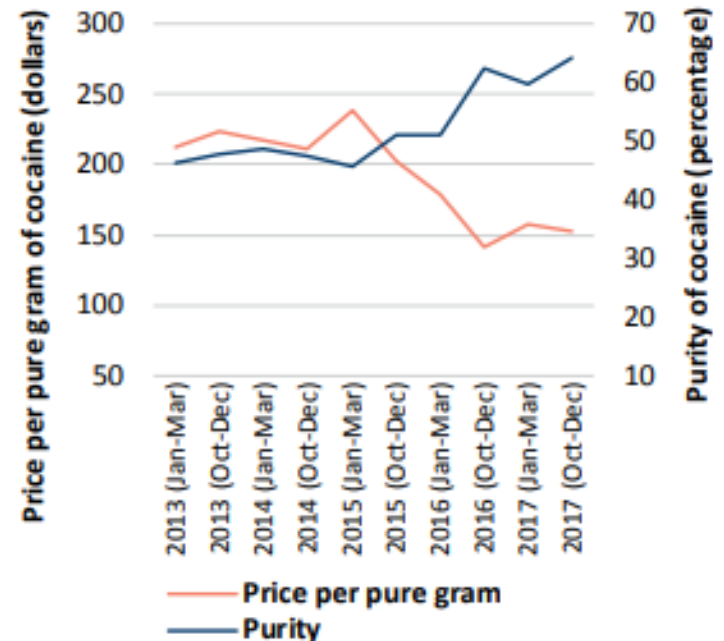
Usage in the USA has become relatively stable while price has gone down, and purity has gone up

**FIG. 20** Trends in the use of cocaine and “crack” cocaine, United States, 2002–2018



Source: United States, Substance Abuse and Mental Health Services Administration, *Key Substance Use and Mental Health Indicators in the United States: Results from the 2018 National Survey on Drug Use and Health: Detailed Tables* (Rockville, Maryland, Center for Behavioral Health Statistics and Quality, 2019).

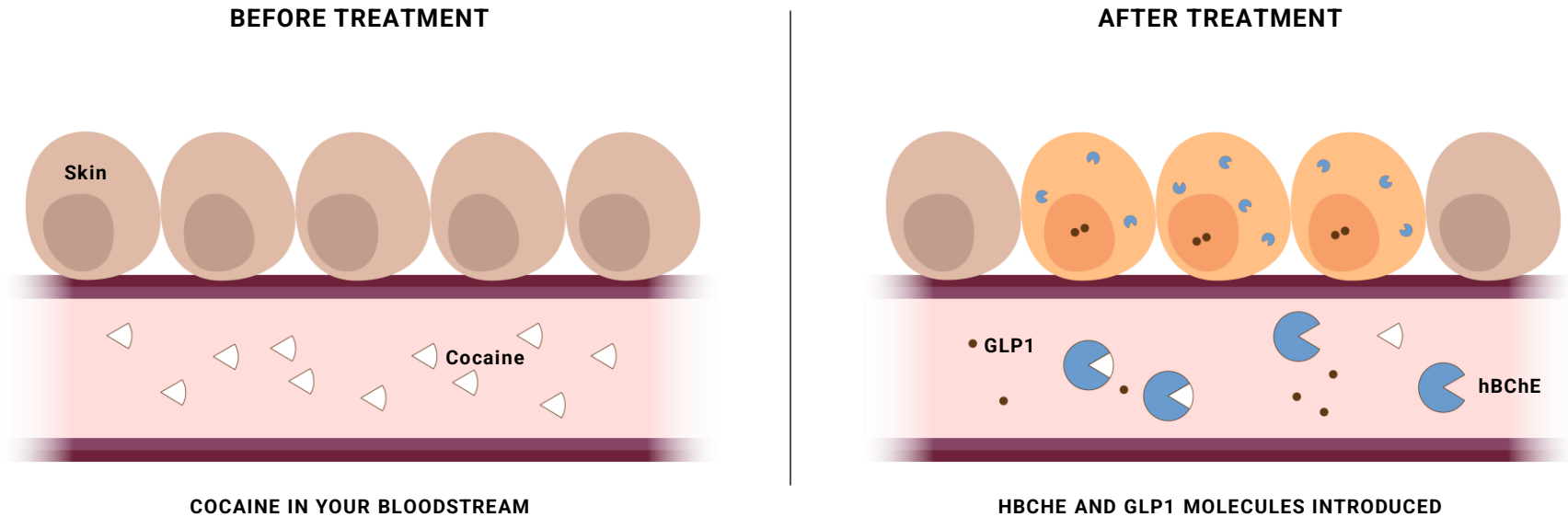
**FIG. 21** Price and purity of cocaine, United States, 2013–2017



Source: United States, Department of Justice, Drug Enforcement Administration, *2019 National Drug Threat Assessment* (December 2019).

# Our Technology - Cocaine

AddGraft Therapeutics' unique treatment for cocaine addiction addresses cocaine in the bloodstream and in the brain



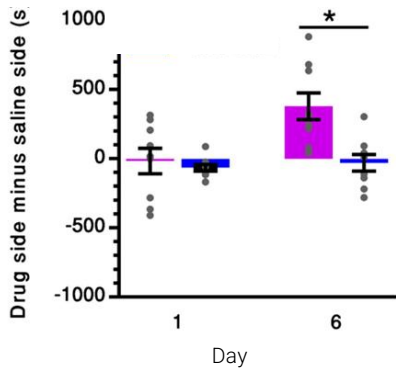
AddGraft Therapeutics' unique treatment utilizes a skin bioengine to deploy natural occurring molecules to treat addiction

# Our Technology – Cocaine

This method for treatment has shown highly encouraging preclinical results and **successfully prevents cocaine addiction, relapse and overdose-related death**

## PREVENTING ADDICTION

**Experiment:** Testing addiction rates in grafted and non grafted mice

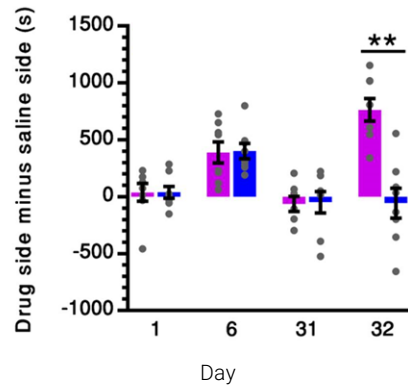


- Not Grafted Mice
- Grafted Mice

**Results:** Addictive behavior not developed in grafted mice

## PREVENTING RELAPSE

**Experiment:** Testing relapse rates in grafted versus non grafted mice

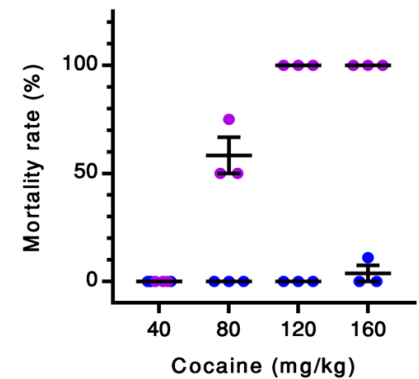


- Not Grafted Mice
- Grafted Mice

**Results:** Formerly addicted mice when grafted did not relapse

## PREVENTING OVERDOSE DEATH

**Experiment:** Testing mortality rates in grafted and non grafted mice



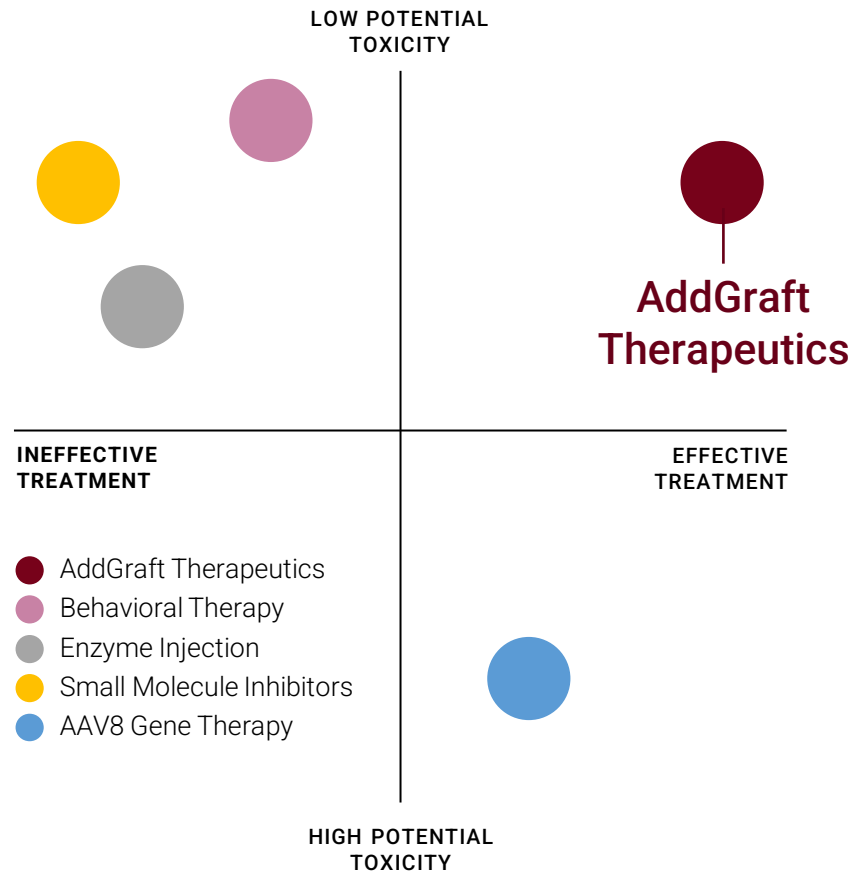
- Not Grafted Mice
- Grafted Mice

**Results:** Grafted mice, exposed to twice the lethal dose of cocaine, did not die or show other effects of drug use

# Market Assessment – Cocaine

Within the cocaine abuse treatment market, **there are no FDA approved treatments**

and those that are being considered, outside of AddGraft Therapeutics, have potential for severe health complications and efficacy issues



# Potential Patient Testimony

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Unfortunately, individuals with cocaine abuse have had little luck with existing treatments and are desperate for new solutions

## Quote (via email reach out)

“Good morning, my son XXX is usually cocaine, I need help for my son his 29 year and use for 6 year. From the bottom of my heart i really would like my son to be included in the human phase the research on.”

“Hello Dr. Xu,

My name is XXX. Over the last 20 years I’ve been fighting with alcohol and cocaine. I have tried to take my life a few times, but there’s something that keep me going. I’ve tried different recovery treatments and nothing works. Cocaine has always won this battle. My last relapse was last week and I’ve spent a few days in the mental disorder unit for drug abuse. I can’t go through this situation once more. **I am tire of my cocaine problem and I’d like to wear out my last chance.** Taking a look through internet, I found an article on your studies and the progress on mice. Is it possible on people?? I don’t want to waist your time, but **I’m willing to try anything. I want to live, but live well and more or less happy.** Thanks a lot for your time, xxx”

“Dear sir, I’m 47 and an active professional with a loving family **who would like to kick a 25 year old habit.** Please consider me”

# Expert Testimony

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Industry experts agree that the current cocaine treatment landscape requires new innovation and that AddGraft's treatment could make a large impact and be commercially accepted

Expert	Position	Quote (Slight Paraphrasing)
Bil Koonar	Director at the John Volken Foundation	<ul style="list-style-type: none"><li>• Would love to be involved in a clinical trial and believes that their patients would be interested</li></ul>
John Wang	MD/PhD Professor, Westport Anesthesia / Missouri Endowed Chair for Research Department(s) of Anesthesiology, Biomedical Sciences UMKC School of Medicine	<ul style="list-style-type: none"><li>• Preventing relapse and overdose is the primary challenge to treating cocaine overdose</li><li>• Would welcome a new treatment even if it did include a simple surgery</li></ul>
Denise Connelly	Co-occurring Disorders Program Facilitator at Sheppard Pratt	<ul style="list-style-type: none"><li>• Current residential treatment center has a minimum of a 20 day stay at \$50k of out of pocket patient expense</li></ul>

# Market Assessment

Within the cocaine abuse treatment market, there are no FDA approved treatments and those that are being considered, outside of AddGraft Therapeutics, have potential for severe health complications and compliance issues



**Behavioral Therapy**



**Enzyme Injection**



**Small Molecule Inhibitors**



**AAV8 Gene Therapy**



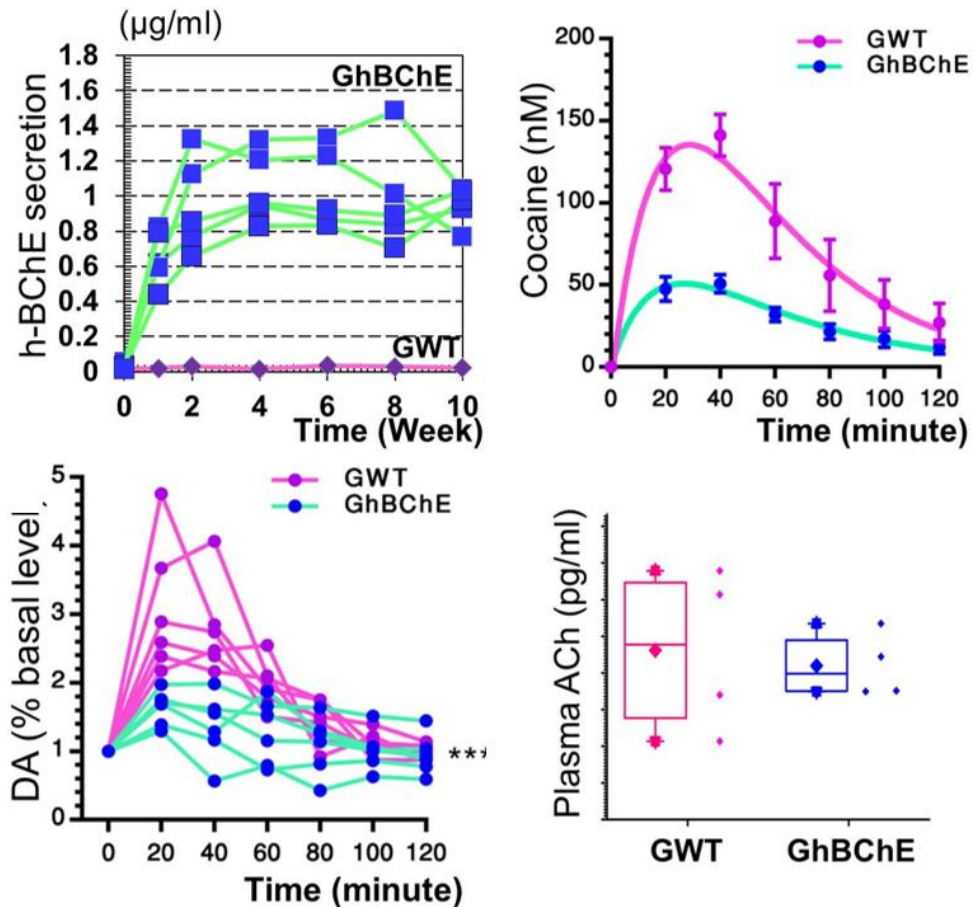
**Skin Graft Gene Therapy**

	Behavioral Therapy	Enzyme Injection	Small Molecule Inhibitors	AAV8 Gene Therapy	Skin Graft Gene Therapy
Frequency	30-90 days	Weekly	Every day	One time	One time
Ease for Patient	—	—	...	...	...
Complication / Toxicity	+	...	...	—	+
Cost	\$50k+/year	\$100k/year	\$4K/year	>\$100k, one-time	\$60K, one-time



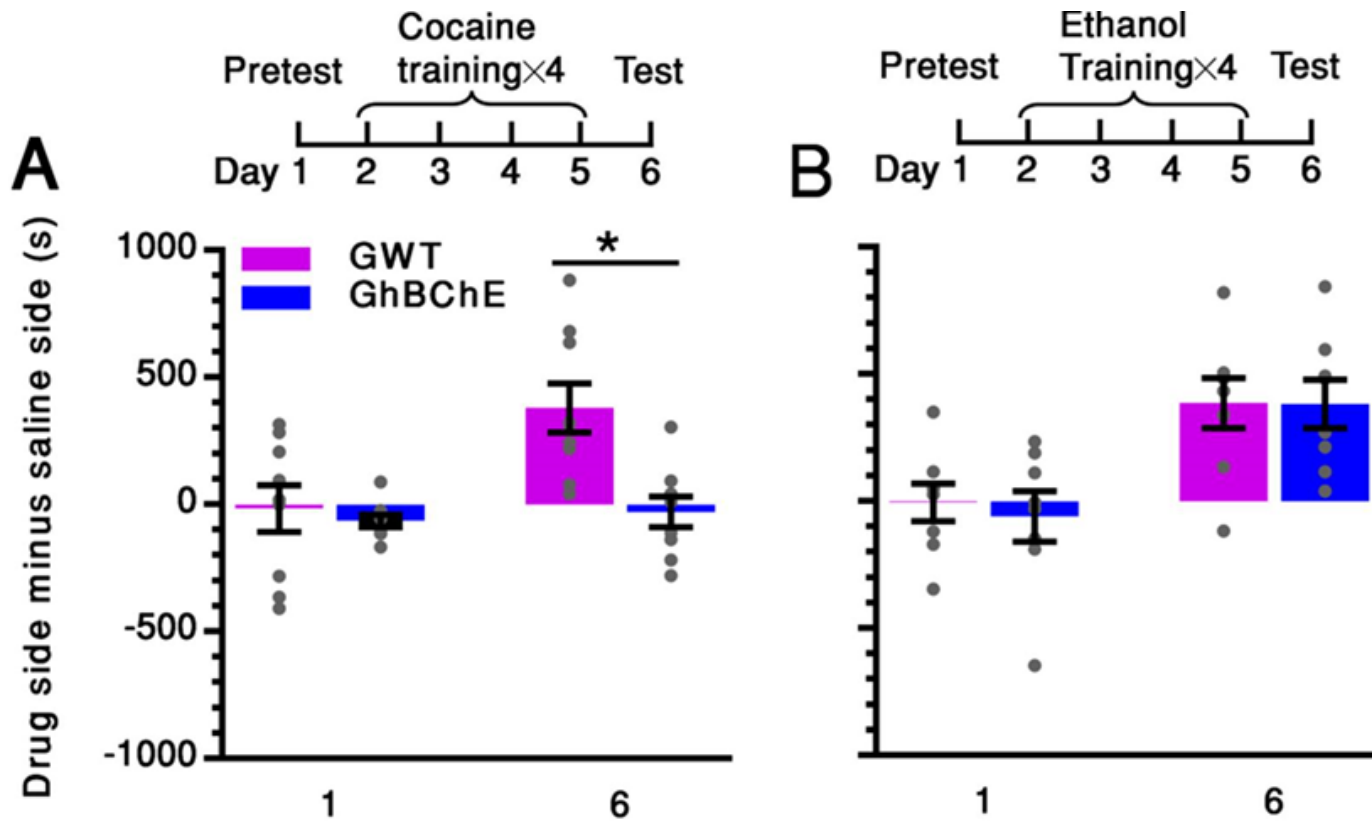
# Our Technology – Scientific Results

hBChE expression reduces cocaine and DA levels in vivo



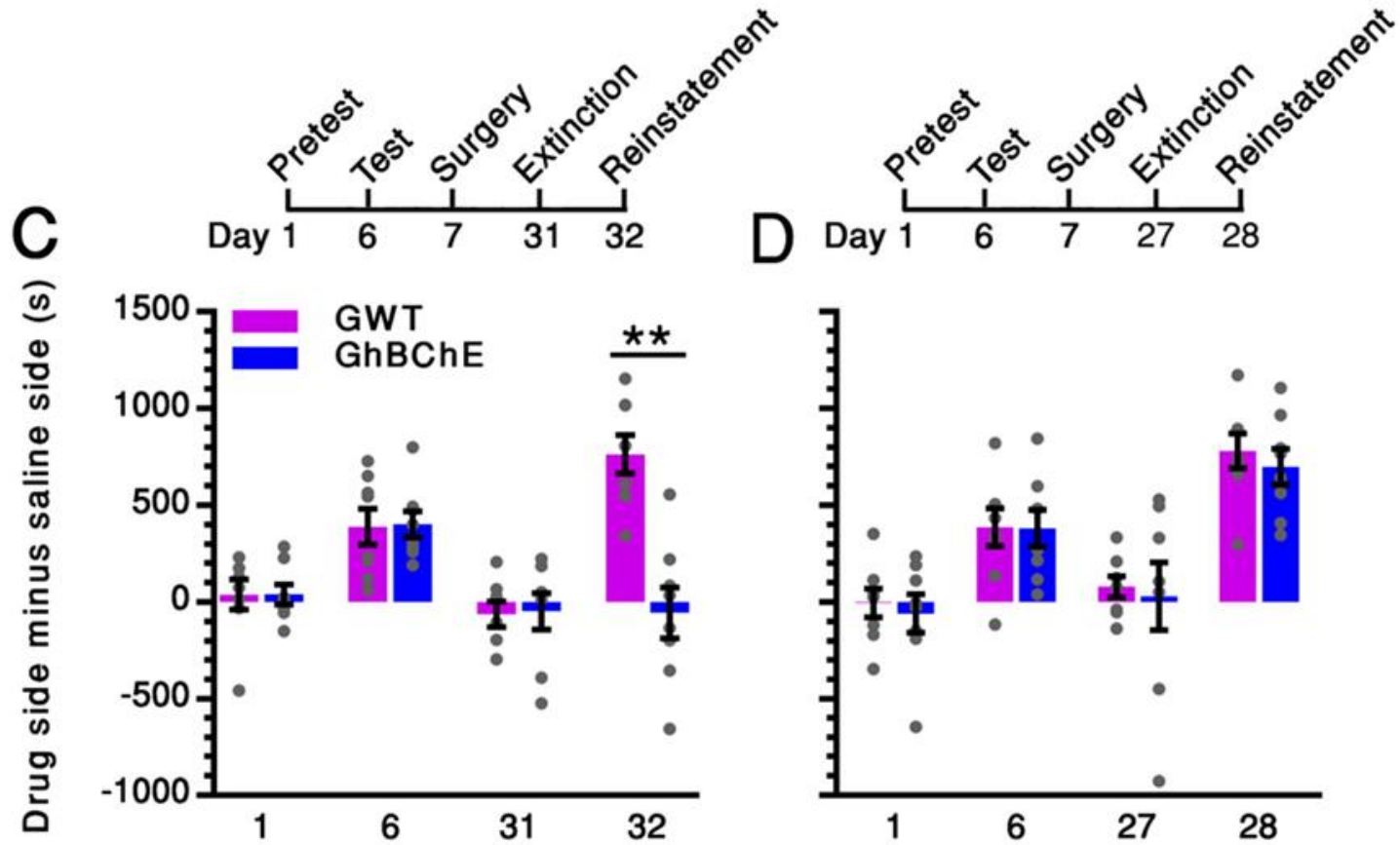
# Our Technology – Scientific Results

GhBChE mice do not develop cocaine- and do develop normal ethanol-induced reward behavior



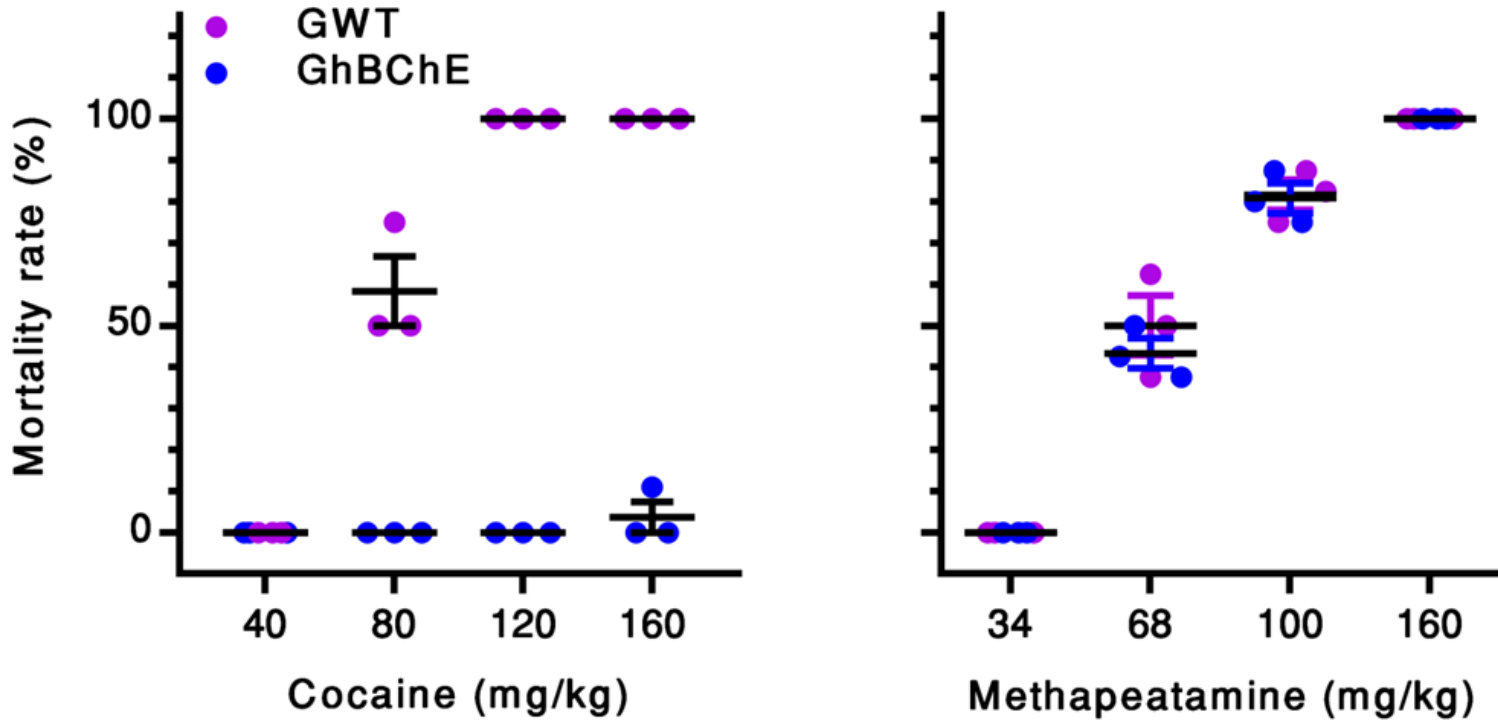
# Our Technology – Scientific Results

Grafting hBChE cells also attenuates cocaine-induced relapse



# Our Technology – Scientific Results

GhBChE mice are insensitive to lethal doses of cocaine but not methamphetamine



# Alcohol and Cocaine Co-Abuse Data

Epidermal stem cell-derived hBChE and GLP1 protect mice from reward and toxicity induced by co-administration of alcohol and cocaine

