Manifest Technologies

Transforming CNS therapeutics through computational neuroimaging
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Team

International leaders in computational psychiatry & clinical neuroimaging.

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  Yale University

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  Head of Business Development
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  Neuroinformatics Engineer
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  Psychiatry
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  Informatics DevOps Director Imaging Tech.
  Psychiatry
  Yale University

- Clara Fonteneau, Ph.D.
  PET Imaging Research Scientist
  Psychiatry
  Yale University
CNS drug development is risky and expensive

$2B
R&D investment required per one new drug

4%
of psychiatry drugs receive approval from preclinical

86%
of clinical trials fail due to unsuitable patients

High cost and failure rates driven by an inability to target specific brain circuits and therefore patients who would benefit most

Harrer et al., 2019, Fogel, 2018
Most assets fail **too late**, driving cost and inefficiency

CNS R&D is failing

Neuro faces the lowest approval rate across drug development

- Psychiatry drugs receive lowest overall approval rates (~4%)
- Phase II-III transition is a key driver of cost & inefficiency (~24%)
- Suboptimal patient enrichment without neural target informed symptoms
- Poor confidence given lack of neural target mapping to symptoms
- Lack of prioritization of agents given poor animal-to-human neural target mapping

Most assets fail too late, driving cost and inefficiency
Manifest solves major cost and efficiency barriers in CNS trials

Our platform automates multimodal animal & human neuroimaging processing and analytics to address key bottlenecks in CNS R&D

- Enrich patient population based on neural target informed symptoms
- Confirm neural target mapping in humans linked to symptoms
- Develop agents with animal-to-human neural target mapping

Data modalities:
- Functional MRI (pharmacological & clinical, resting-state & task)
- Structural MRI (T1w/T2w myelin, diffusion)
- PET
- EEG/MEG
- Transcriptomics
- Symptom scales
- Other phenotypic measures
Manifest transforms asset development

**Develop** agents with animal-to-human neural target mapping

**Confirm** neural target mapping in humans linked to symptoms

**Enrich** patient population based on neural target informed symptoms

~$0.5 – 1B+

Pipeline value driven by increasing likelihood of approval & accelerated development

Source: https://bioheights.com/ra-npv-forecast-calculator/

**Improve success rate & efficiency**

# of drug candidates in development

Preclinical | Phase I | Phase II | Phase III | Phase IV & Rx

MANIFEST TECHNOLOGIES, INC.
10+ years of innovation at Yale laid NAIO’s foundation

Commercial collaborations around clinical neuroimaging.

$2M NIH Director’s Award for computational neuroimaging at Yale.

2012

2016

$12M NIH grant to Yale to deploy TRANSCENDS - a multi-site human neuroimaging clinical trial and informatics platform.

2019

Patent awarded for human computational neuroimaging.

2018

$12M NIH grant to Yale to deploy TRANSCENDS - a multi-site human neuroimaging clinical trial and informatics platform.

https://clinicaltrials.gov/ct/show/N2CT04457310
Manifest can fundamentally alter the success of a clinical trial

Status Quo

- No patient enrichment strategy

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<tr>
<th>Effect size</th>
<th>Required sample size</th>
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<td>0.17</td>
<td>411</td>
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- Our ML-optimized clinical enrichment score drives precise patient selection, would have enriched the trial with high responders

- Therefore, using our proprietary patented approach a failed depression trial would have been successful with better power, resulting in less time and lower cost

WEAK EFFECT NECESSITATES MANY TRIAL PARTICIPANTS

STRONG EFFECT NECESSITATES FAR FEWER PARTICIPANTS
Q & A

Thank you for your attention

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