
From: jeffrey E. <jeevacation@gmail.com>
Sent: Tuesday, August 29, 2017 9:58 AM
To: [REDACTED]
Subject: Re: Alzheimer's

well done

On Tue, Aug 29, 2017 at 1:28 AM, [REDACTED] <[REDACTED]> <mailto:[REDACTED]> > wrote:

FYI

----- Forwarded message -----

From: [REDACTED] <Bill and Larry - hi. =nd just to you both - I will send to the others and copy Larry later tonig=t. <mailto:[REDACTED]>

Given my experience building and managing learning initiatives and my understanding of this landscape, I've tried to think about your competitive/comparative advantage while giving you=a little more time to learn in the background.

At the end of this learning you could exit the space easily, go deeper or even change strategies based on what you learn. In 2-3 years a few things will unfold - and I would just caution you to tread lightly because all sorts of new data is emerging - not only about mechanisms of disease but about whether AD is a distinct pathologic entity. Lord knows = I just don't want you to get caught into a=polio type vortex until you are ready.

McKinsey has been hired to help build your strategy and I will pass all of this along to the McKinsey team, Bose and Jonah under separate cover. I will also continue to support them, make introductions and join their sessions - next one September 8. In my honest opinion, McKinsey maybe not the right partner but we will all rally behind them.

<=pan style="line-height:115%">

See you both soon... [REDACTED]

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Aspiration

1. Segment the landscape until we have a natural advantage
2. Opportunities small enough to win, large enough to matter
3. Measurable points on the board

Situation

- Alzheimer is not a typical disease with a single causal factor / etiology
- Polarized scientific community
- No shortage of R&D resources
- Requires longitudinal investments in health and hard to quantitatively track pathology
- What needs fixing

o =A0 Institutions – processes, policies

o =A0 Tools & technologies – validation, standardization

o =C2 Science – exploration, cross-sector ideas

Informed Entry into Alzheimer's Landscape

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\$100 million, 3 year learning initiative managed quietly from bgc3 that will explore:

1. Performance of existing institutions vs. need for creation of new (or hybridized) ones
2. Opportunities for cost savings and market building
3. Barriers to clinical trial participation
4. Processes for data sharing and standardization
5. Novel mechanistic approaches

Specific Targets for Exploration

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Target 1: Underwrite risk for private sector; keep data in the public domain

\$20 million

AMC-AD,=National Institutes on Aging (NIA)

Matchin= grant (1:2 for government, 1:1 for private sector)

Propose= Outcomes

<=ont face="verdana, sans-serif">· In 3 years, study and trial data for 2016++ pipeline fully public and curated by NIA<=pan>

=font face="verdana, sans-serif">· Stronger NIA

=font face="verdana, sans-serif">· Open trial data=/span>

- 10 new candidate drugs put into later stage discovery process

Cost

Recipie=

Form

Possibl= Partner: IMI

Propose= Outcomes

<=ont face="verdana, sans-serif">· In 3 years, 5 validate biomarkers

=font face="verdana, sans-serif">· Standardized validation processes

=font face="verdana, sans-serif">· Open and shared trial and registry data

- Aligned US/Europe regulatory and study processes

What we=learn

<=ont face="verdana, sans-serif">· Coherence of standards

=font face="verdana, sans-serif">· Appetite for shared data

- Ability of new institution to attract additional resources

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<=ont face="verdana, sans-serif">Target 3: Build microbiomic fundamentals

\$20 million across 3 recipients

Recipient=

1. \$5m to NIA/NIH to RFP pre-inflammatory and inflammatory markers (\$5m)
2. \$5m to ICDDR,B to classify non-pathogenic colonists and create a digital library <=span>
3. \$10m TBC via BMGF to redraw bacterial taxonomy based on genetic criteria to supplement traditional identification and classification<=p>
Grants =span>

Propose= Outcomes

<=ont face="verdana, sans-serif">· Identify non-pathogenic colonist strains for use in health and also food and supplement industry=span>

=font face="verdana, sans-serif">· World Gut library

- Update bacterial classification systems to include genomics<=font>

What we=learn

<=ont face="verdana, sans-serif">· Build a deeper understanding of the microbiome with applications across health, pharma and food sciences

=font face="verdana, sans-serif">· Modern bacterial taxonomy based on genetic characteristics</=ont>

- Microbiome non-pathogenic library offers biomarkers for health but also potential prebiotic and probiotic candidates for food and pharmaceutical industry= (monetizable = creates new market)

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<=ont face="verdana, sans-serif">Target 4: Invest in computational repurposing of failed candidate drugs

\$18 million

TBC

1. \$1m scoping (go/no go) effort with McKinsey
2. \$2m pilot
3. \$15m initial investment in repurposing fund either as part of a new entity versus within the NIA AMP-AD

1 contract, 1 grant and 1 investment

Propose= Outcomes

<=ont face="verdana, sans-serif">· Scope potential of market and collaboration with McKinsey

=font face="verdana, sans-serif">· 20 repurposed medications

- Creates new market opportunity for failed drugs

Target 5: Investigate and build social biomarkers correlated with aging and dementia

\$2 mill=on

Israel =rain Technologies

Grant f=r Grand Challenge-style competition

What we=learn

- Scale and scope of potential for digital biomarkers in cognitive disease

<=ont face="verdana, sans-serif">Target 6: Bring the financial industry into the conversation

\$1 mill=on

\$1 mill=on to Dr. Jason Karlawish at University of Pennsylvania Medical School / Wharton School <=font>

Grant

What we=learn

- Possibility of using financial markets to reduce cost and ease burden of care
- Create a new financial product
- Create automated checks and balances or financial standards for demented adults or retiree= over age 65 with cognitive challenges
- Share actuarial burden between long term facility care-caregivers

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<=ont face="verdana, sans-serif">Target 7: Reduce CMS facility and hospital admission costs

\$1 mill=on

RAND

Grant

What we=learn

- Save tons of money
- Reduce hospital admissions
- Share burden of care

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<=ont face="verdana, sans-serif">Target 8: Improve trial enrollment<=span>

\$2 mill=on

Lon Sch=eider, USC School of Medicine

Grant

Propose= Outcomes

<=ont face="verdana, sans-serif">· Linkage across trials

=font face="verdana, sans-serif">· Improved (and shared) recruiting tools

=font face="verdana, sans-serif">· Corporate advocacy

· Involvement of search engines (Google, Bing, etc) in stacking searches

What we=learn

<=ont face="verdana, sans-serif">· Barriers to participation

=font face="verdana, sans-serif">· Corporate appetite to contribute

· Institutional appetite to widen trials and/or share controls=/p>

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<=ont face="verdana, sans-serif">Target 9: Novel mechanisms for exploration

\$25 mil=ion

Either =ia intermediary such as Cure Alzheimer's Fund or 8-10 individual recipients (see below)<=span>

Grant

What we=learn

<=ont face="verdana, sans-serif">· Dysregulation of neural pH dynamics: Aimee Kao, Ph.D. / University of California, San Francisco

=font face="verdana, sans-serif">· Human age equivalency and functional phenotypes: Fred "Rusty" Gage, Ph.D.=/ Salk Institute for Biological Studies

=font face="verdana, sans-serif">· Gliovascular changes and waste (glymphatics): Jeffrey Iliff, Ph.D. and William Rooney, Ph.D. / Oregon Health & Science University=/p>

=font face="verdana, sans-serif">· White matter dysfunction as a biosensor: Ragnhildur Thóra Káradóttir, P=.D. / University of Cambridge

=font face="verdana, sans-serif">> Cellular networks controlling proteinopathy: Martin Kampmann, Ph.D., Michael Keise=, Ph.D., David Kokel, Ph.D. / University of California, San Francisco=/span>

=font face="verdana, sans-serif">> Immunological gating pathways and denegeration: Dr. Michael Schwartz / Weizmann Institu=

=font face="verdana, sans-serif">> Rejuvenation of the nervous and vascular systems: Dr. Shai Efrati / Sagol Center

· Filamentous bacteriophages as therapeutics: Proclara biosciences (may be better fit f=r DDF)

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<=ont face="verdana, sans-serif">Target 10: Convene a 3 year Task Force to guide your learning

\$ 1 mil=ion

NACC, D=. Bud Kukull / University of Washington

Grant

What we=learn

<=ont face="verdana, sans-serif">> Expert opinion(s) on emerging data, trends and science

· Progress and perspective on our own learning from Targets 1-9 as listed above

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Man=ging the Process

\$ 500,0=0 per year

TBC

Contrac=or or Staff (bgC3) as under the radar manager or advisor + .25 FTE administrative support

Propose= Process

<=ont face="verdana, sans-serif">> Perform due diligence on proposals

=font face="verdana, sans-serif">> Manage portfolio of learning grants (and contracts)</=ont>

=font face="verdana, sans-serif">> Report to Bose/Jonah/Larry quarterly or as required otherwise</=ont>

=font face="verdana, sans-serif">> Attend or delegate attendance for major meetings

=font face="verdana, sans-serif">> Submit quarterly summary report and annual learning report</=ont>

· Serve as primary point of contact with partners / quarterly calls

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=A0 please note

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