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SiNON Therapeutics

"Carbon Dot"

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SiNON Therapeutics patented Carbon Dot is the trojan horse for pharma which shepherds medicine across the "Blood Brain Barrier" (BBB). We are dedicated to improving the lives of women and families who suffer from neurological diseases by refining drug-localization of medicine to the brain.

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5

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Executive Summary

With over 14 years of combined scientific research experience in fields ranging from nanochemistry to radiation oncology; and degrees in medicine, neuroscience, biochemistry, microbiology, engineering, and business – the SiNON Therapeutics team is well poised to tackle the challenges presented in this proposal. Our small size makes us nimble and responsive, while our experience gives us the ability to execute and exceed expectations.

SiNON is dedicated to improving the lives of those who suffer from debilitating neurological diseases by increasing the ability of drugs to cross the Blood Brain Barrier (BBB). Our patented nanoparticle, the Carbon Dot, will enable pharmaceutical companies to encapsulate their drugs in a way which dramatically improves drug-localization to the brain. This allows for a reduction in overall dose administration to the patient, leading to reduced toxicity risk and side-effects while improving therapeutic index and cost-efficacy. Considering the rapid growth of the senior population, and subsequent increase in neurological disease, we believe that our novel technology is an essential part of the overall solution to this healthcare crisis in the US and around the world.

Business Description & Problem We are Solving

Unmet Need

The blood brain barrier (BBB) is a highly selective physical and chemical boundary limiting the access of chemicals, molecules, organisms, and drugs to the brain. Although this barrier is vital in protecting us from bacteria and neurotoxins, it poses a serious challenge from a clinical standpoint when it hinders the passage of administered diagnostic markers and pharmaceutical drugs and limits their therapeutic potential. Basically, clinicians must prescribe much higher doses of a certain drug for that drug to cross the BBB and have a therapeutic effect on the brain. In many circumstances, the higher dose required leads to toxically high levels outside the brain (peripherally) before reaching therapeutic levels inside the brain. Numerous drugs have failed clinical trials or deemed not suitable for human use because of their inability to cross the BBB and subsequent slow uptake into the central nervous system. Furthermore, many drugs currently on the market cause serious peripheral side-effects because of the high dose required to cross the BBB. If one were able to bypass the BBB and therefore administer a lower dose to achieve the same therapeutic effect, this would significantly reduce peripheral side-effects and widen the gamut of drugs available for use.

The BBB blocks 100% of large neurotheraupeutics and 98% of small-molecule-drugs. Current methods exist for bypassing the BBB for purposes of drug delivery, yet they are either ineffective, dangerous, or extremely invasive. For example, the use of bradykinin (a vasodilator) or osmotic disruption are dangerous to the patient because they can change the blood flow in the brain and temporarily reduce the BBB's "blocking ability" to allow for the transport of the drug. It is apparent how dangerous these methods are for the patient because they temporarily allow the passage of foreign and potentially harmful substances to the brain and can induce life-threatening changes in cerebral blood flow. Other methods for crossing the BBB are costly such as high-frequency ultrasound or extremely invasive, such as the surgical implantation of drug delivery devices inside the brain.

Target Customers & Target Drugs

While we consider the end-customers or consumers of SiNON to be any users of a drug encapsulated using SiNON carbon dot technology to pass the BBB, the direct customers will be pharmaceutical companies. SiNON can be marketed to a variety of pharmaceutical companies for use in conjunction with drugs that are intended to target the brain. This includes new and existing drugs.

With pharmaceutical companies as our potential customers, it's intuitive to segment by drugs. Pharmaceutical companies may have existing drugs that would benefit from SiNON technology, drugs in development that would benefit from SiNON technology, or drugs that have not been developed because of the issue with

crossing the BBB. While the future of SiNON may include expansion to add value to a broad portfolio of drugs, our primary goal is to understand which of these drugs. SiNON should target for the immediate future.

SiNON will take into account the following factors to ideally target drugs for which:

- SiNON will add the largest value which is a function of:
    - Number of end-customers, value conveyed to end-customers and ease of use
- SiNON has a high probability of success
- SiNON can be incorporated into the drug more:
    - Quickly, cheaply and easily

Given limited resources, SiNON should look to target a few drugs. Having multiple drugs insulates SiNON from the risk of a single drug failing trials. With improved estimates of costs and success probability SiNON can refine a target portfolio of drugs to pursue for the immediate future. One tool used to quantitatively aid the decision making of which drugs to include is a decision tree analysis. The appendix shows a decision tree cost-benefit analysis for one drug. Similar cost-benefit analyses can be performed for other potential drugs and aggregated to valuate SiNON as a company with a portfolio of drug opportunities.

When looking at what type of drugs to target we considered 3 types:

1) Proven drugs - These are drugs that are FDA approved, but would benefit from SiNON's technology. Reference the decision tree cost-benefit analysis appendix for Paclitaxel a common generic drug used in chemotherapy. Encapsulation of Paclitaxel with SiNON could improve results of chemotherapy targeting brain cancer.
2) Drugs that failed phase 2 testing - We want to consider targeting drugs that might pass FDA testing with the help of SiNON technology.
3) Pre-Clinical Drugs - These are drugs that have not gone through clinical trials.

To discuss which drugs SiNON should target, we must first understand that any drug must go through clinical trials with SiNON encapsulation to be approved with SiNON encapsulations. This means that previously proven drugs used in conjunction with SiNON must go through clinical trials again with SiNON encapsulation. This also means that drugs with less clinical testing experience present a greater risk of failure since there is a risk that the drug itself will fail regardless of the performance of the SiNON technology. The key advantage of targeting a proven drug is that there is a known history of the drug and therefore a higher probability of success. Meanwhile drugs that failed phase 2, but could potentially pass with the help of SiNON may represent a large opportunity to the pharmaceutical companies developing them and present a lower risk than pre-clinical drugs. Meanwhile, the high risk of pre-clinical drugs makes them undesirable target drugs for the immediate future.

While it is important to recognize that our delivery system can transport almost any drug through the BBB and therefore would be applicable to a very wide range of neurological disease, we have opted to discuss only one in the interest of time. We have selected one neurological disease, Alzheimer disease, to demonstrate the potential impact of improved penetration of existing pharmaceutical therapy through the BBB

Sample Neurological Disease

Alzheimer disease, the most common form of dementia, is a severely debilitating disorder of cognitive and behavioral impairment that significantly reduces quality of life and functional status. Currently, it is incurable, yet not terminal, meaning patients suffer a long and progressive course of the disease. The memory loss and confusion makes it difficult for patients to pay bills, care for themselves, recognize family members, or communicate. These symptoms also lead to agitation and depression, eventual weight-loss and death. Because this is a disease that affects the elderly, as society around the world ages rapidly, Alzheimer's will become even more prevalent than it is today.

Currently there are an estimated 36 million with Alzheimer disease. However, by 2050 the estimated number is expected to reach 115 million. It is the 6th leading cause of death in US. Alzheimer's claims more lives each year than both prostate and breast cancers combined. It is currently the only cause of death on the top 10 list for which there is presently no preventive measure, cure, or way to stop the progression of the disease. Alzheimer's is the most expensive disease in terms of its cost in care for the nation. In 2014, the estimated cost of care was $214 billion and by 2050 this cost is expected to reach $1.2 trillion dollars.

Market Size

According to BCC Research, BBB technology, a sub-industry of the pharmaceutical sector, amounted to $21.8 Million in 2013. The sub-industry is estimated to grow to $471.5 Million by 2019. These estimates pertain to sales of the technology through the supplier side rather than encompassing the billions in sales foreseen by the greater pharmaceutical industry in development of new/enhanced medications. These estimates are conservative because they take into account the slow recovery of the global economy and the desire for investors to preserve capital. In 2014, there were three compounds in the clinical development pipeline using BBB technology, and this will grow to around eight by 2019. Pharmaceutical sales patterns predict 85% of BBB technology sales in 2019 will be from US sales and Europe will account for 15% or less.

The current barriers to entry in this market include the following:

- Securing investment capital.
- Regulatory agency approval.
- Lack of existing knowledge sharing and partnerships among sub-industry, which hinders technological advancement.
- High abandon rate, due to inability to pass the BBB.

Instead of developing BBB technology in-house the emerging pharmaceutical model is to license or acquire this expertise. With a small number of players currently in this market, BBB technology companies can have power over buyers (pharmaceutical companies) if their delivery method is determined to be the most efficacious/safe over competitors.

Distribution Channels

Since Carbon Dot is a vehicle for drugs to cross the blood brain barrier, we will pursue a B2B strategy. Our natural channel of distribution will be the pharmacological and biotech companies. We intend to partner or license the Carbon Dot to these companies who will serve as a Value Added Reseller. Licensing the Carbon Dot to manufacturers of block buster drugs for neurological disorders will help them extend their current market exclusivity as well. An alternative channel is a B2C strategy where SiNON licenses the drugs from manufacturers, encapsulate it with the Carbon Dot and sell it directly to patients. Drugs that failed phase 2 testing will be potential targets since they can be licensed at a lower cost compared to proven drugs which are FDA approved. This strategy will involve significant expenses to cover costs of clinical trials and marketing campaigns to educate providers, payers and patients.

Other Applications:

- **Parkinson's Disease (PD)**: PD is a disorder affecting dopamine producing neurons in basal ganglia of the brain. It is progressive, affects movements, balance, facial expression, cognition and may result in depression. 96% of patients are over 50 years old when diagnosed. Global burden of PD is estimated to be currently 7-10 million with 60,000 Americans diagnosed with PD each year. With increasing life expectancy, the disease prevalence is only expected to increase.

  Financial burden of PD in US is estimated to be $25 billion per year, factoring in the direct and indirect/opportunity costs of lost income. Medications cost $2500 per patient per year and surgery costs $100,000 per patient. (http://www.pdf.org/en/parkinson_statistics)

Since dopamine does not cross BBB, it's precursor levodopa which otherwise crosses BBB is currently used to treat PD. Levodopa has other systemic side effects such as nausea, dry mouth, dyskinesia (abnormal movements) etc. Also, levodopa has to be co-administered with carbidopa (Trade mark: SINEMET) to prevent its break down to dopamine in the blood stream. So, dopamine can be encapsulated with the Carbon Dot to facilitate BBB penetration and avoid the systemic side effects of Levodopa.

- **Bacterial Meningitis:** Infection of lining of the brain and spinal cord by bacteria is called bacterial meningitis.
  (Penetration of drugs through the blood-cerebrospinal fluid/blood-brain barrier for treatment of central nervous system infections; Nau R, Sörgel F, Eiffert H; Clin Microbiol Rev. 2010;23(4):858.)

  This is a very serious condition with a case fatality rate of 25% for adults and upto 28% of survivors could have permanent neurological morbidity.
  (Community-acquired bacterial meningitis: risk stratification for adverse clinical outcome and effect of antibiotic timing; Aronin SI, Peduzzi P, Quagliarello VJ; Ann Intern Med. 1998;129(11):862.)

  In non-disease states, most beta lactam antibiotics cannot penetrate the BBB. During meningitis, there is separation of intercellular tight junctions which facilitates antibiotic penetration into the cerebro spinal fluid (CSF). However, as the inflammation reduces, the antibiotic penetration also decreases. As a result of this, very high doses of antibiotics have to be given intravenously to facilitate adequate CSF concentration. This high dose is associated with significant systemic toxicities such as low blood counts, clostridium difficile colitis which can in turn delay recovery or even increase mortality. Encapsulating antibiotics with Carbon Dot can facilitate easy penetration of BBB, ensure consistent CSF concentration without the need for high doses and hence reducing systemic toxicities.

- **CNS oncology:** Incidence of brain tumors is 28.6 for 100,000 adults and 5.6 pre 100,000 children. 5 year survival rate for these malignancies are 34%.
  (CBTRUS Statistical Report: Primary Brain and Central Nervous System Tumors Diagnosed in the United States in 2008-2012; Ostrom QT, Gittleman H, Fulop J, Liu M, Blanda R, Kromer C, Wolinsky Y, Kruchko C, Barnholtz-Sloan JS; Neuro Oncol. 2015 Oct;17 Suppl 4:iv1-iv62. Epub 2015 Oct 27.)

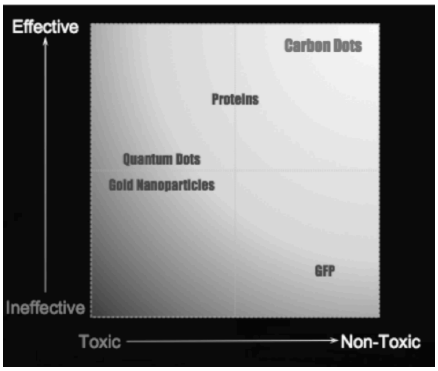
  Transportation of drug across BBB and blood tumor barrier (BTB) is the most important factor affecting drug delivery to the brain tumor. Though BBB is disrupted around the tumor site, corticosteroids used to treat edema or swelling around the tumor will partially re-establish BBB thus reducing the likelihood of the tumor responding to chemotherapy. So, high dose chemotherapy is a strategy used to enhance drug delivery to the tumor. This is again associated with multiple systemic toxicities depending the chemotherapeutic agent used.

  Carbon Dot can be used as a vehicle to effortlessly penetrate BBB, target these tumors, increase their efficacy and probably improve survival.

Competitive Analysis

Competitive Advantage

SiNON Therapeutics has developed a novel method of crossing the blood brain barrier, which is effective, non-invasive, and most importantly can be utilized by almost all drugs (making even retroactive application possible).



Our solution, the Carbon Dot (US Patent #12/719,791), is a nanoparticle made of the non-metal compound Carbon. This complex nanoparticle is simply explained as a capsule, with a hollow core that can transport drug molecules, diagnostic markers, or almost any substance into the brain.

One key aspect of the Carbon Dot is the ability to attach chemical functional groups to the surface of the "capsule". Attaching different functional groups allows us to change the solubility, and therefore the rate of passage across the blood brain barrier, of the Carbon Dot. Also, the more soluble Carbon Dots are easily excreted by the kidneys, which make this delivery system safe (it does not linger in the body). Different functional groups can also act as a "zip code" and target the Carbon Dot to specific areas of the brain.

Sustainable Competitive Advantage

Current solutions at various stages of development include a variety of drug delivery mechanisms that have greater targeted delivery. These include virus, bacteria, nano-particles, etc. Some companies focus specifically on oncology and cancer related treatments, while others focus on Alzheimer's treatments.

There is significantly more research and data available on virus and bacterial models of drug delivery mechanisms as these are more commonly used for the broader population. Another drug-delivery mechanism uses plastic, which accumulates in the brain after doing targeted drug delivery, which leads to toxicity. Our carbon dot can not only cross the BBB, but it also does not leave any waste like the aforementioned product, making it ideal for treating brain diseases.

Direct Competitors

As far as the market we are targeting is concerned, alternative solutions that are non-invasive include lipidizing the drug. The water -soluble parts of the drugs restricts BBB transport conversion of water-soluble drug into lipid-soluble pro drug is the traditional chemistry driven solution to the BBB problem. Probes Encapsulated by Biologically Localized Embedding (pebbles). They designed the pebbles to carry a variety of agents on their surface, each with a unique function. Testing focused on brain cancer. Virtually all small-molecule neuroprotective agents have failed in clinical stroke trials because either (a) these molecules have unfavorable safety profiles or (b) the drugs do not cross the BBB.

Alternatives

There are many delivery vehicles some of which include liposomes, micelles and dendrimers, biodegradable particles and nanoparticles.

Competitive Landscape

Despite the vast untapped potential in the growing central nervous system therapeutic markets, there are still a few players due to the complexity.

Currently, the potential BBB technologies are:

- A vehicle platform technology.
- A type of drug technology that enables passage across the BBB that also changes compounds or requires certain combinations of compounds to co-exist. BBB technology (by Type)
- Receptor mediated transport
    - Passive (diffusion) or Active (catalyzed) transport
- Carrier mediated transport, that includes:
    - Carrier-mediated transporters (CMT), such as glucose and amino acid carriers.
    - Receptor-mediated transport (RMT) or transcytosis, such as insulin or transferrin.
    - Interactions with (including blocking of) active efflux transporters, such as pglycoprotein.

Methods to cross the BBB

- Biological/Chemical Transport, Physical Force (Energetic) Transport

Companies in the Competitive Space

- Ablynx, a drug company is developing a form of antibody therapy

- Transmolecular
- Other companies Allon Therapeutics, OptiNose, Protheragen and MedInvent are creating drugs that specifically circumvent the BBB through the nose.
- Another source of penetrating the BBB is through non-invasive low-frequency ultrasound using equipment/device (ExAblate) from InSightec
- Other potential competitors in the drug delivery system development: ArmaGen, Angiochem, Adenios, BiOasis, Insightec (ultrasound-opening of the BBB), Nanomerics, NeuroVive, NsGene, Ossianix, Pharmidex, to-BBB, Vect-Horus, XenoPort, and Xigen.

*Note: See Appendix for BBB Technology companies and respective technology method

Competitive Forces Analysis

SWOT Analysis

The table below highlights the strengths and weaknesses within the company and the opportunities and threats that are external to the company.

Strengths	**Weaknesses**
• Unique value proposition (Carbon Dot) • Highly qualified team with diverse background (medicine, neuroscience, biochemistry, etc.) • Capability to carry drugs for a wide variety of neurological diseases	• Low Cash on Hand • Time to profitability due to the number of clinical trial phases • Potential patent infringements
Opportunities	**Threats**
• New Partnerships with leading Pharmaceutical companies • Perceived as an innovative company • Strategic acquisition by one of big players • Growing market. Fewer players (BBB)	• Dependence on business partners to transport Carbon Dot • Rapid technological changes and increased complexity • Potential new entrants / Growing competition • Evolution of the Healthcare industry

(*See appendix V for details)

Key Challenges, Risks & Issues

- **Technical Risk Accuracy:** Given the sensitivity of the profession, precision is of paramount importance. Though the proposed solution is novel and we are confident to carry it through, it's yet to be proved through a series of clinical trials. There is a risk associated with designing, implementing and / or integrating (drugs with the 'capsule') end to end solution correctly for the first time.
  Mitigation Plan: Strategic alliance / partnership with leading pharmaceutical companies

- **Financial:** Low cash on hand. Long time until profitable due to the number of clinical trial phases
  Mitigation Plan: Licensing (less lucrative option), Leverage Buyout (LBO) and VC (investors).

- **Value Capture (E.G., Risk of Imitation):** Although the barrier to entry is high due to complexities, the risk of imitation is significant. In addition, big and mature players can leverage their 'presence' in the market to penetrate in this highly niche area.
  Mitigation Plan: Continue the patent route, exclusive contracts, and move with speed.

- **Competitive Threats:** Currently the landscape is not highly competitive. However, due to potentially very high growth and rewarding area, mature companies can quickly advance leveraging current capabilities.
  Mitigation Plan: Accept the risk. Develop the solution right the first time and quickly grab the market share.
- **Market Risk:** Difficulty in recruiting and retaining key partners. Also, political and economic conditions may affect our partners' businesses and their ability to continue to invest in this endeavor.
  Mitigation Plan: Multiple partners to diversify and reduce risk.

Reimbursement Landscape

To seek reimbursement for our technology we have several options. One option is to sell it once it is partially or fully developed. The benefit of this option is it allows us to have an exit strategy favorable to our investors seeking a quick return on their investment. Another benefit is that we would not have to take on the risk of scaling up our development/manufacturing, and deal with further research and development expenditures or post marketing adverse events/risks.

A second option would be to develop a medication along with the technology to take to market, such as a medication for Alzheimer's disease. A recent trend in the pharmaceutical industry involves licensing compounds. We could license a compound from another pharmaceutical company and bring it to the market along with our technology. In this case, we would seek reimbursement from negotiated contracts with both public and private insurance companies. This option could be the most lucrative in the long term, but is the least feasible given our resources. This option is also riskier because we would have to deal with developing a drug to bring to market which could take years of research, and millions, if not billions, in funding. In addition, we would need to develop a marketing strategy to inform physicians about our medication. In this case, we would need to either contract or develop a sales force which requires additional funding.

The option we have decided to be optimally lucrative and feasible is to license our technology to pharmaceutical companies once it is developed. Licensing allows us to stay in the industry and continue to develop this and other products. Our main goal will be to license our technology to large Pharma companies. Pfizer, which has proven blockbuster medications, such as Aricept for Alzheimer's, would be highly interested in our technology because they could receive an extension on their current patent with our novel drug delivery method. The largest risk we face with this option is obsolescence through competition, which is a risk we face with any of the other options as well.

The objectives form the framework for the operating plan and also determine its financing needs and strategy.

There are two main sets of objectives:
It is anticipated that the startup lifecycle will last approximately 30 months from initiation to exit. The initial Carbon Dots technology was developed over the course of the past 12 months and there are four key stages of research and development required prior to licensing the completed technology in early 2017.

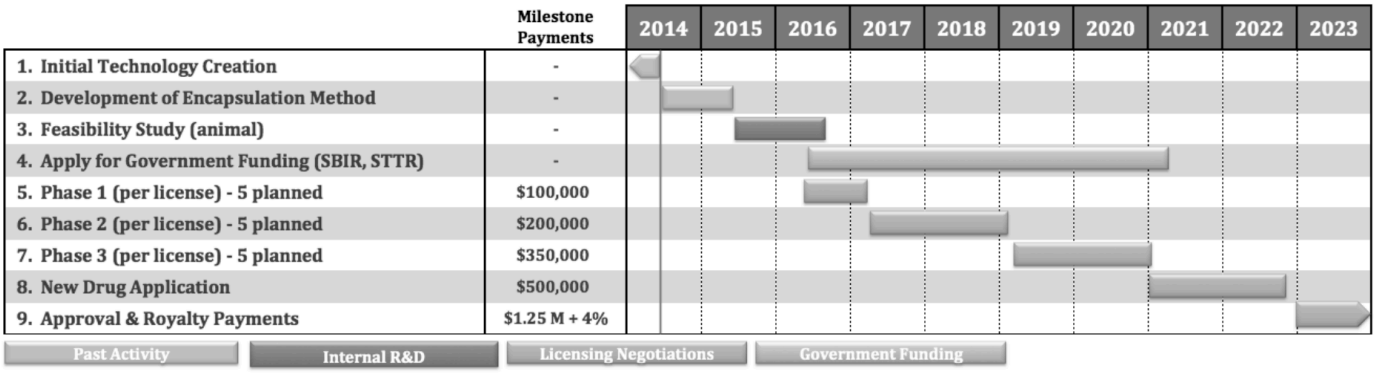
The major milestones for the company's planning horizon (most likely somewhere between two and five years depending on the nature of the business). Milestones will normally include prototype, product, clinical milestones, first customer acceptance, major partnerships, etc. These will be the major events or achievements that mark important steps in the development and significant reductions in the risk of the company.

The technology that remains to be developed includes the actual delivery mechanism of the carbon dots (intramuscular, intravenous, arterial, oral.. etc) to the patient. Various methods of infusion and intake will need to be tested to determine if there are any toxicities or changes in the efficacy in crossing the BBB. Furthermore, supply chain issues will need to be addressed to determine whether the product is temperature/dust sensitive and whether delays in use would reduce the efficacy and shorten the shelf life of the carbon dots. The shelf life of

the powdered form of the carbon dots is about 2-3 years and would depend on whichever drug is being encapsulated, this shelf-life may need to be tested with various drugs for FDA compliance. The biggest technology development remaining is the timing of drug release and location of drug release (decapsulation). It is important that the drug delivery be timed so that the carbon dots have appropriately crossed the BBB. Furthermore, the location of decapsulation can be targeted using antibodies to help the drug reach specific areas in the brain. These are more complex mechanisms and will need animal testing further down the line. All of these technological developments will go through traditional FDA clinical phase testing.

The financials required for each phase of testing are represented in the graph below. These numbers are based on industry averages as there is not much data on getting a product like this to market. The first phase of the project will involve animal studies for biodistribution and quantification of various drugs we encapsulate, this will take 3-4 months. The second phase involves cell line studies to test the release (decapsulation) mechanism in the target site, which could take 2-3 months. The most in-depth and difficult phase will be the third animal test which will take what we learn in the cell-line studies to test the decapsulation process in live animals. This could take up to 6 months depending on our success rate. The exit strategy as aforementioned would be to license this technology to existing pharmaceutical companies or sell the intellectual-property entirely. Thus far, we have not had any outside investors and probably will not have any investors until after the decapsulation animal study results are complete.

Financials & Milestone



Initial Technology Creation: The initial technology development. Will serve as the foundation for future R&D to be conducted by the team.
Development of Encapsulations Method: Lab-based study will be used to develop the generic drug encapsulation and de-encapsulation methods.
Animal Study 1 &2: The initial animal study is anticipated to take approximately two to three months and will utilize a mouse model to test bio-distribution and quantification.
Cell Line Study: Test release mechanism in cell lines to set a protocol rather than in animals as it will significantly reduce costs.
Animal Study 3: The third animal study is anticipated to take approximately four to six months and will utilize a mouse model to test targeted neural therapy for a relevant disease such as brain tumor.
Capital Raise: Additional capital will be required to complete the last animal study. It is anticipated that the cost of the studies will be approximately $500K. This process will involve the engagement of one or more external investors and will be supported by the positive outcomes of the cell line study. The cost of the clinical trials will be the pharmaceutical company's cost.
Licensing Negotiations: The final stage of the startup process involves marketing of the technology to a broad range of potential clients, primarily comprised of large-scale pharmaceutical companies. The startup exit will occur upon completion of a final licensing agreement.

EXIT: WE PLAN TO HAVE OUR EXIT WITHIN 4-6 YEARS AT THE END OF PHASE 2 TRIALS WHERE A PHARMA COMPANY WOULD EITHER ACQUIRE US OR SIGN AN EXCLUSIVE LICENSING DEAL.

Appendix I

Team Members

Afreen Allam (Founder & CEO): a recent graduate from Duke's Fuqua School of Business, has over 7 years of research in nanomedicine. Her extensive studies on applications of carbon nanotechnology in drug delivery and bioimaging led to the patent of the Carbon Dot in 2013. She is a graduate of North Carolina State University with a double major in microbiology and biochemistry and holds a masters degree in finance and banking, she has also conducted cell-line studies at Johns Hopkins. At the age of 17 Afreen had her first DNA sequence published and filed a patent at the age of 20. She has presented at numerous biomedical conferences including the Drugs & Diagnostics Conference, Biotech Research Symposium, and National Tech Connect Conference. She was recently invited to be a moderator at a large innovation conference.

Dr. S. Sarkar (Chief Scientific Officer): completed his PhD in Chemistry in 1975. He did his Post-Doctoral Research project at University of Dortmund, Germany and University of Belfield, Germany. He joined IIT-Kanpur as a Lecturer in the Department of Chemistry in 1978. He has been a visiting Scientist and Professor to various universities in US and Germany. He was invited to lecture at several National and International Conferences. His research interests are metalloenzymes, transition metals, Metal Clusters-Supramolecular Chemistry, Fullerene and Bio-inorganic chemistry. Presently he is Professor Emeritus at BESUS, Botanic Garden-711103, Howrah , India.

Abdul Allam (Director of R&D): Mr. Allam focuses on product of carbon nanomaterial which includes multiwalled carbon nanotubes, carbon dots, and graphene. Masters in Organic Chemistry and Masters of Business Administration from Ottawa, Canada.

Mr. Bholanath Pakhira (Lead PhD Researcher): Is responsible to conduct innovative synthesis , purification and solubilization of carbon nano particulates based on sizes. He has studied taxol – nano carbon conjugation. He is M.Sc. from Indian Institute of Technology Kanpur and presently a CSIR pre-doctoral Research Fellow in the Department of Chemistry at BESUS and doing PhD under Professor S. Sarkar at BESUS (Kolkata, India)

Sameer Berry (Medical Student Liaison): has a track record of dedicating his time to improve the lives of patients with neurological disease. He is currently in the MBA/HSM (health sector management) program at Duke's Fuqua School of Business and finishing his medical doctorate (M.D.) in Michigan. Sameer graduated cum laude with a degree in Neuroscience at Northeastern University where he conducted neurological research at Harvard Medical School and was a founding editor of Northeastern's Science Magazine. Since then, he has authored more than 11 publications in high-impact journals and received national grant funding and awards for his research. His business experience includes co founding a charity which provided Neurological Stroke health education to more than 1500 people in India and developing the Alzheimer's memory-care protocols at 4 assisted-living facilities in California.

Advisors

Dr. Tage Honore: Holds a masters in pharmacy, doctoral degrees in Medicinal Chemistry and Neurobiology. He's also had business training from Harvard Business School and European Management Center. Tage has had an extensive background within pharma and life sciences. He

founded Aestus Partners in 2004 and Aestus Therapeutics in 2006. Tage has contributed and/or directed teams to bring 40 new molecular entities into and through clinical studies. His background includes development and implementation networks to help obtain increased pipeline productivity in several pharmaceutical companies.

Dr. Jeremy Petranka: Petranka comes from a background in consulting (has worked for multiple Fortune 100 companies) and strategy roles. He has helped companies to align their information technology with their business strategies. He has now shifted into focusing on managerial decision-making and business strategy. He has won many teaching awards and has served as a mentor for many entrepreneurial students. He is currently an associate professor at Duke, The Fuqua School of Business. He received his PhD in Economics from UNC.

Dr. Jon Fjeld: Executive direction for the Center of Entrepreneurship and Innovation at Duke. He has been teaching courses in entrepreneurship and strategy at Fuqua since 2005. Fjeld obtained his MA and PhD from the University of Toronto and his MBA at Duke University. Prior to coming to Fuqua Fjeld spent over twenty years in marketing, engineering and general managements in both start-ups and public companies.

Doug Eisner: Duke MBA class of 2007, is the former owner of GrassRoots Biotechnology. He successfully sold his company, GrassRoots, to Monsanto. Before that, he grew company to 25 employees with over $4 million in revenue.

Appendix II

BBB Technology Companies and Respective Technological Method

Company	Technology Description	Technology Type
Ablynx	A human BBB transmigrating antibody fragment derived from a llama antibody selectively binding to an antigen on the surface of cerebromicrovascular endothelial cells expressing BBB antigens that is in the preclinical stage for Alzheimer's.	RMT
Angiochem	Engineered peptide compounds (EPiC) cross the BBB via the LRP1 transporter that, when combined with Paclitaxel (ANG 105), tumor progression has been halted in recurrent brain cancer (in phase II studies).	RMT
ArmaGen	Antibody engineered to recognize insulin to cross BBB via transcytosis that is in phase I/II, first for Mucopolysaccharidosis (MPS) Type I, or Hurler's syndrome. Financing and further development is with Boehringer Ingelheim Venture Fund, Shire, Takeda Ventures, Mitsui and Global Investment	RMT

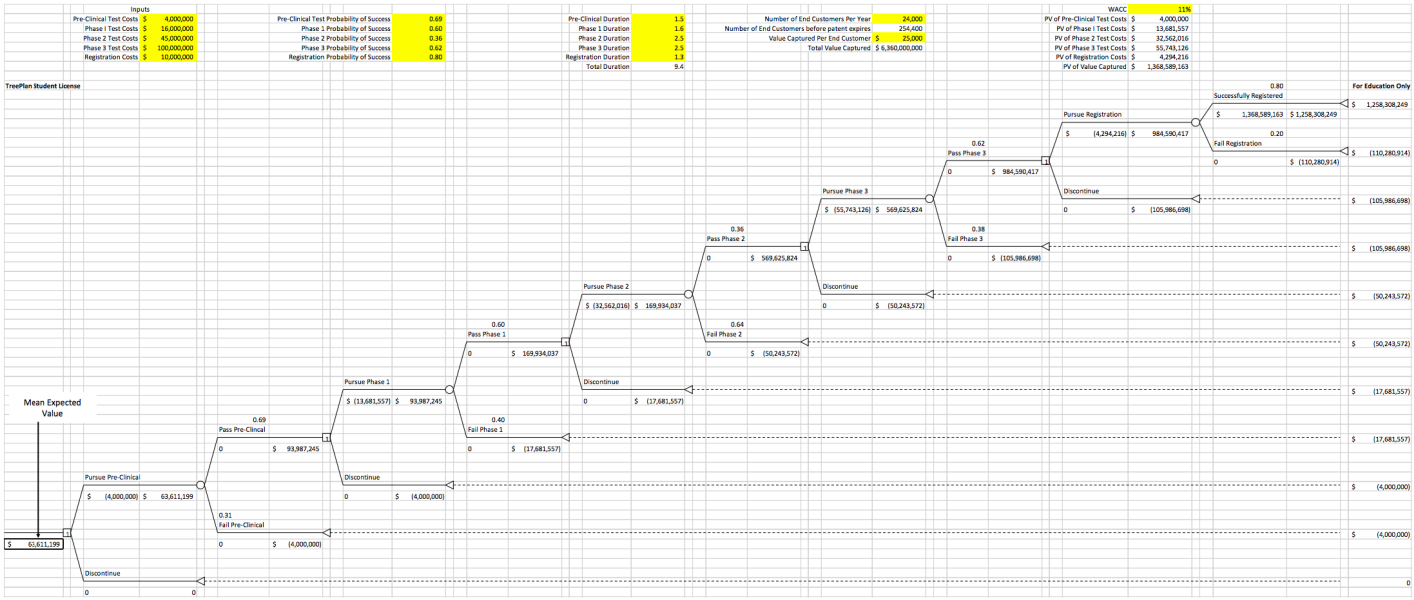
BiOasis	Naturally occurring protein p97 (serum melanotransferrin) is used as carrier to move compounds across the BBB via transferrin receptor that has proof of concept completed for two brain chemotherapeutics.	RMT
Pharmidex/ Genzyme	Cerense technology creates oligoglycerolipids that can deliver compounds up to 250,000 daltons, including proteins, through BBB transporters.	Undisclosed
Lundbeck/Ossianix	Lundbeck: fund in a joint alliance development of Ossianix's Blood Brain Barrier targeting technology for the development of bispecific biopharmaceuticals to treat CNS disorders. Ossianix: has a single domain antibody platform takes its inspiration from a shark model.	Undisclosed
Lundbeck/Nanomerics	3-year collaboration begun in April 2014 Nanomerics will designed a polymer nanoparticle to bring a Lundbeck compound across the BBB	Undisclosed
NsGene	NsGene's Brain Repair-NGF platform (NsGene0202) currently in clinical testing. The initial results have validated the safety, tolerability and technical feasibility of this therapy. Preclinical safety studies are in progress through a grant by the Michael J Fox Foundation for Parkinson's Research for NsGene 0301 for the first clinical study in patients with Parkinson's disease in 2014. NsGene uses its proprietary Brain Repair technology to deliver GDNF directly in the brain. It helps enhance dopamine production.	Alternative to RMT (Implant with Drug)
Roche/Raptor Pharmaceuticals	Roche is in preclinical with a Brain Shuttle module that is an antibody fragment to pass through the transferrin receptor for anti-amyloid effect for Alzheimer's. Roche currently has exclusive rights to Raptor's NeuroTrans. There has been preclinical work done to conjugate it to a variety of protein drugs, including enzymes and growth factors. Studies have shown that radiolabeled NeuroTrans may be transcytosed across the BBB.	RMT
To-BBB	To-BBB has G-Technology, which means it is working to combine drugs with pegylated liposomes with the endogenous tripeptide glutathione as a targeting ligand.	RMT

Vect-Horus	Peptide-vectors optimized at the pharmacological level (cleavable or labile bonds, cleavable disulfide bonds, coupling via a spacer arm, etc.) transport a molecule via transcytosis that is in preclinical stage.	RMT

Appendix III

SiNON Potential Customer Decision Tree-Cost Benefit Analysis

Overview:

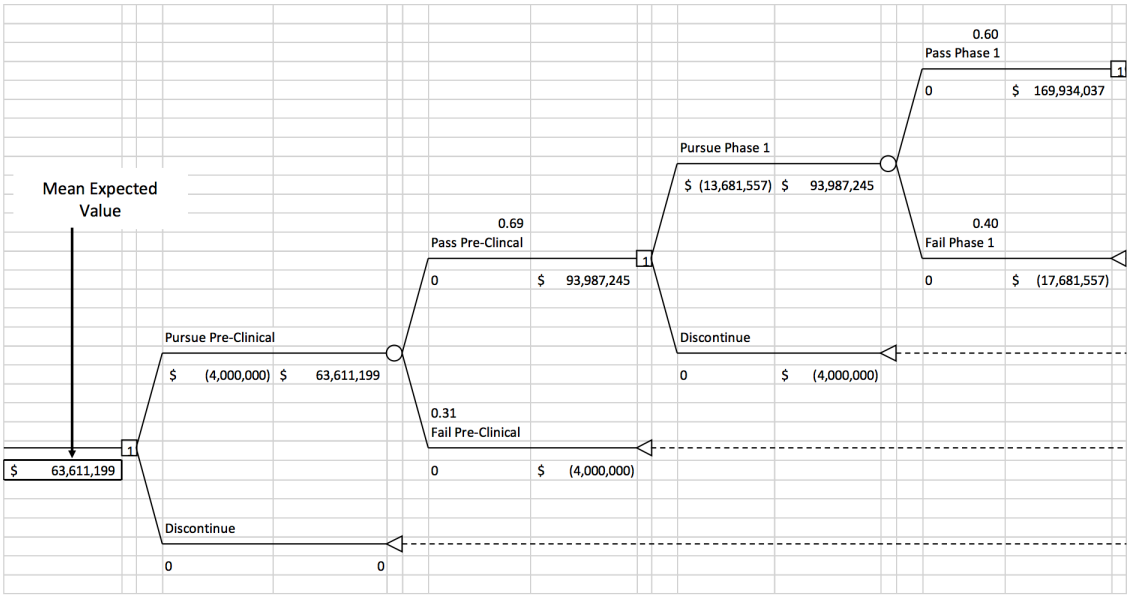


Decision Tree Detail Views:

Inputs

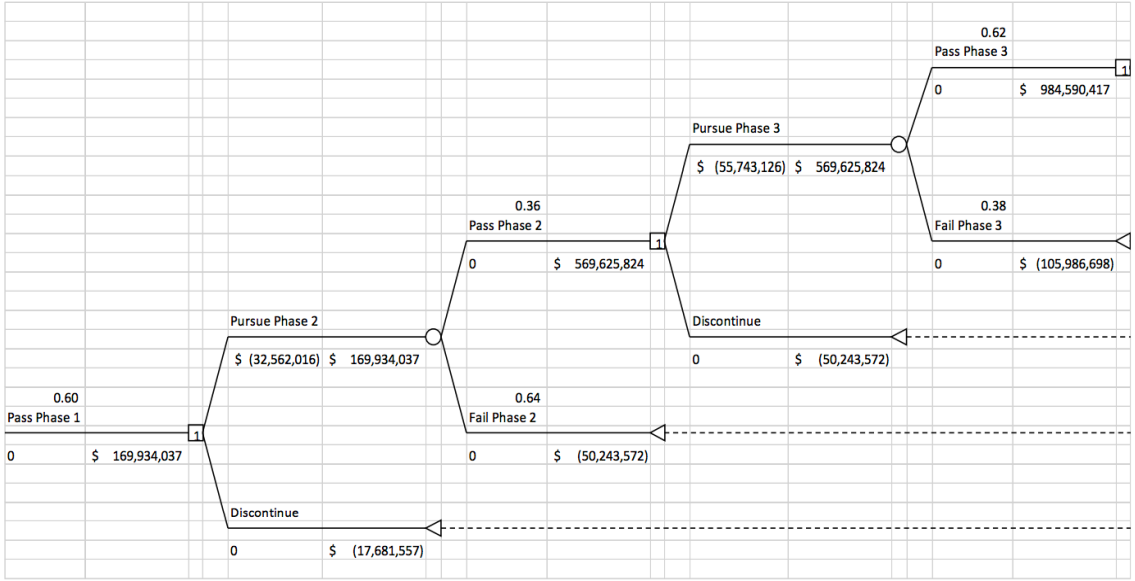
Pre Clinical Test Costs	$ 4,000,000
Phase 1 Test Costs	$ 16,000,000
Phase 2 Test Costs	$ 45,000,000
Phase 3 Test Costs	$100,000,000
Registration Costs	$ 10,000,000

Pre Clinical Test Probability of Success	0.69
Phase 1 Probability of Success	0.60
Phase 2 Probability of Success	0.36
Phase 3 Probability of Success	0.62
Registration Probability of Success	0.80

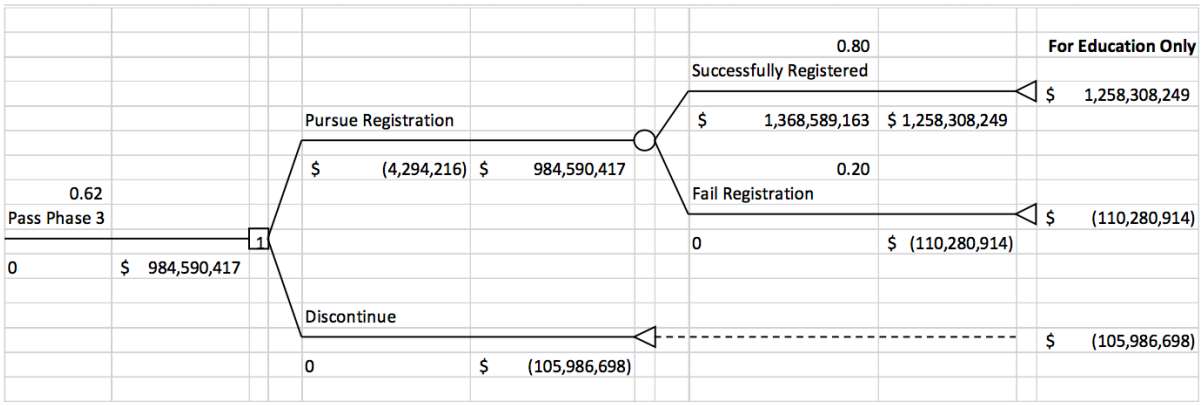


Pre Clinical Duration	1.5
Phase 1 Duration	1.6
Phase 2 Duration	2.5
Phase 3 Duration	2.5
Registration Duration	1.3
Total Duration	9.4

WACC	11%
PV of Pre-Clinical Test Costs	$ 4,000,000
PV of Phase 1 Test Costs	$13,681,557
PV of Phase 2 Test Costs	$32,562,016
PV of Phase 3 Test Costs	$55,743.126
PV of Registration Costs	$4,294,216
PV of Value Captured	$1,368589,163

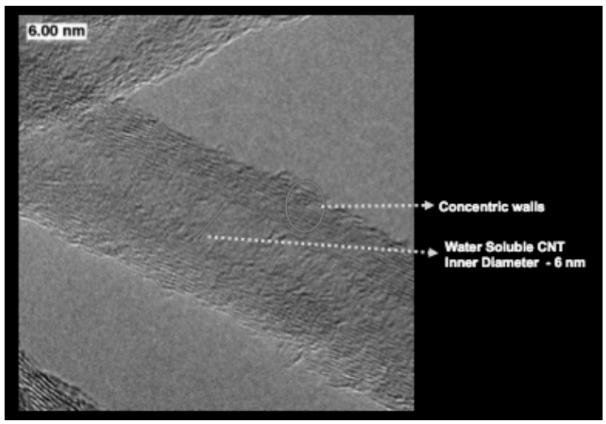


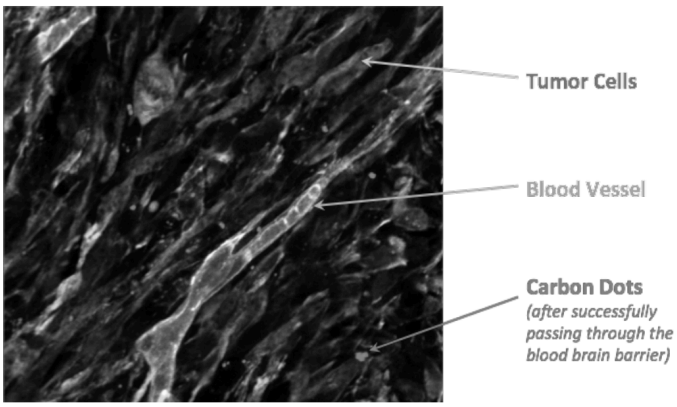
Number of End Customers Per Year	24,000
Number of End Customers Before Patent Expires	254,400
Value Captured Per End Customer	$ 25,000
Total Value Captured	$ 6,360,000,000



Appendix IV

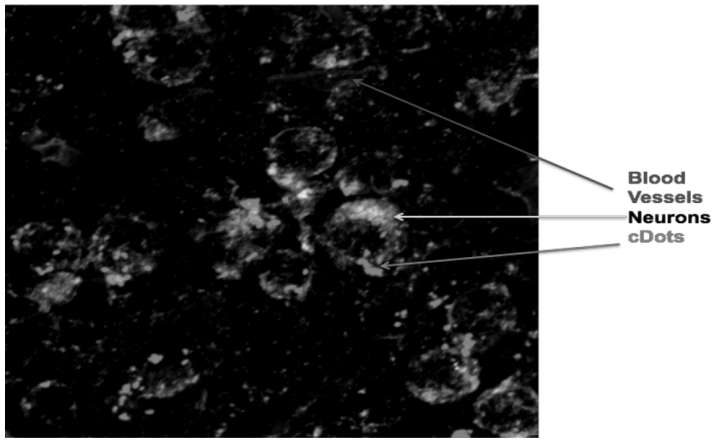
Previous Tests: This SEM image shows the multi-layers of the Carbon Nanotube (starting material of CDots). It has a inner chamber where drugs or genes can be encapsulated. Also on the surface of the walls there are carboxylic groups that you can do surface conjugations with specific receptors.





This test was done on a Glioblastoma (most aggressive form of brain tumor). If the nanoparticles (CDots) were not able to pass the blood brain barrier (BBB) all the red dots would be seen in the white blood vessel. Also, we were able to get a good uniform distribution within the brain. This is what we were hoping to see.

We also saw that the CDots tend to aggregate towards the neurons. This will particularly be important if we choose to treat a disease like Alzheimer's since that's where you need the medication to get to.



Features	**Quantum**	**Gold Nanoparticles**	**Green Fluorescing Proteins**	**Proteins**	**Carbon Dots**
Water Solubility	No	Yes	Yes	Yes	**Yes**
Toxicity	Yes	Yes	No	No	**No**
Target Drug Delivery	Yes – with Wrapper	Yes – with Wrapper	Yes-with modifications and not widely used	Yes-with modifications ; must be altered for each drug	**Yes-without wrapper**
Bio-Imagining /Fluorescence	Yes with wrapper. Under biofluid unwrapping may release toxic Q.Dots	Yes – with wrapper. Under bio-fluid the unwrapping may expose metallic gold particle	Yes-but short lived	No	**Yes without wrapper. Excrete spontaneously from the body. There is no wrapping & the Cromoz C.Dots are non-toxic.**

The Pink Ceiling
Statement of Support

SiNON is focused on solving an area with a high unmet need, neurology. Due to the lack of drugs being able to penetrate the blood-brain barrier (BBB) and high dosages given there is a high risk for systemic toxicity. Take for example Alzheimer's Disease, knowing that two-thirds of Alzheimer's patients are women,[1] SiNON is dedicated to improving the quality of life for not only these patients but also the 10 million women caregivers.[1] SiNON's goal is to make medications safer by targeting specific organs (in this case the brain) to localize delivery. By doing so they can significantly reduce inefficacy and toxicity. Winning InnovateHER will help with the next stages for fundraising to begin their efficacy and release model studies in animals. With their new data SiNON can move forward to working on their strategic pharmaceutical partnerships.

Afreen Allam, is a vibrant CEO who graduated with a MBA from Duke's Fuqua School of Business, and has spent over seven years of research in nanomedicine. As of today she has raised over $575,000 in funding and taken first place at the Duke Start-up Challenge, the Duke Angel Award and NC idea grant.

We received 41 applications from Santa Barbara to Pennsylvania, who completed an online application. The five finalists then competed on site at The Pink Ceiling's Raleigh Office. Our diverse finalists included:

- NeuroVice - an oral device for epileptic patients
- SuperVize - children's wearable tech that tracks individuals in a group's location
- Safe - an application to help reduce the risk of transmitting sexually transmitted diseases
- Elliegrid - a smart pill box.

Over 150 people attended the event and 3,100+ viewed on Facebook Live. Our judges included Academy Award Nominated Filmmaker Star + Director of "Super Size me" Morgan Spurlock, Bethany Edwards founder of LIA diagnostics, and angel investors Suzanne Charnas and Doug Eckert. Multiple media outlets were in the room including: ExitEvent, Triangle Business Journal, WRAL Techwire, and North State Journal (print). Each finalist will also be showcased by the Case Foundation's #FaceOfFounders Campaign, expected to release the week of June 26, 2017. We will be sure to pass along the features.

ExitEvent: https://www.exitevent.com/2017/06/innovateher-5-startups-pitch-products-for-women-created-by-women/

Triangle Business Journal: http://www.bizjournals.com/triangle/news/2017/06/01/rtp-startup-advances-to-national-innovateher-pitch.html

WRAL TechWire: http://wraltechwire.com/sinon-therapeutics-advances-in-innovateher-competition/16735797/

1: Alzheimer's Association. 2017 Alzheimer's Disease Facts and Figures. Alzheimers