Synaptogenix, Inc.
Investor Update Call
July 26, 2022

Presenters
Bob Weinstein – CFO
Dr. Alan Tuchman – Chief Executive Officer
Dr. Daniel Alkon – President and Founding Chief Scientific Officer

Q&A Participants
Joanne Lee – Maxim Group
Jason McCarthy – Maxim Group
Chin Lyn – Lyn Asset Management
Tucker Anderson – Above All Advisors
Tom Bishop – BI Research
Larry Stoffman -- LDS
Private Investor
Robert Smith – The Center for Performance Investing
Chuck – Richland
Jack Mayer – Private Investor
John Bowden – Private Investor
Mason Holt – Private Investor

Operator
Greetings. Welcome to Synaptogenix Investor Update Call.

At this time, all participants are in a listen-only mode. A question-and-answer session will follow the formal presentation. If anyone should require operator assistance during the conference, please press "*", "0" on your telephone keypad.

Please note, this conference is being recorded.

I will now turn the conference over to Bob Weinstein, CFO. Thank you. You may begin.

Bob Weinstein
Thank you. Good afternoon and thank you for joining our Synaptogenix, Inc., Conference Call.

We plan to discuss our recently announced open label dose optimization trial, as well as our ongoing NIH sponsored Phase II clinical trial.

My name is Bob Weinstein. I'm the CFO of Synaptogenix and will be hosting our call, today.

With me are our Chief Executive Officer, Dr. Alan Tuchman, and our President and Founding Chief Scientific Officer, Dr. Daniel Alkon.

I'd like to remind everyone that today's call is being recorded. A replay of today's call will be available by using the telephone numbers and conference ID provided in our press release.

I'd also like to call your attention to the customary Safe Harbor disclosure regarding forward-looking information.

The conference call today will contain certain forward-looking statements, including statements regarding the goals, strategies, beliefs, expectations and future potential results of Synaptogenix including, without limitation, the expected timing of our clinical programs and the expected announcement of clinical trial results.

While our management believes these statements are reasonable based upon estimates, assumptions and projections, as of today, Tuesday, July 26, 2022, these statements are not a guarantee of future performance.

Actual results may differ, materially, as a result of risks, uncertainties and other factors, including but not limited to the factors set forth in the company's filings with the Securities and Exchange Commission.

Synaptogenix undertakes no obligation to update or revise any of these forward-looking statements.

I now turn our call over to Dr. Tuchman for a few words.

Alan Tuchman
Thank you, Bob. I want to welcome everyone to this clinical program update, which we're pleased to present to you, today.

The highlights of our discussion today and today's primary focus is our ongoing six-month duration NIH sponsored Phase II trial for the treatment of moderate to moderately severe Alzheimer's disease.

The trial is fully enrolled and currently on schedule for announcing topline data, during the fourth quarter of this year.

The trial was developed and modified, based upon previous trial experience that we gleaned from our two previous Phase II clinical trials.

This trial is double-blinded, placebo controlled and twice the length of our previous trials. We believe the extended duration will provide additional time for the placebo group to decline,

which will give us a much better chance of highlighting positive and significant results from the treatment of Bryostatin with our patient group.

Dr. Alkon is going to go into further details regarding this trial.

Last week, we announced dosing of our first patient in an open label optimization trial. While our current dosing has been found to provide clear, cognitive improvement over baseline, the goal of this trial is to optimize the extent and duration of these benefits.

We also announced, earlier today, the reformation of our scientific advisory board, comprised of industry and academic leaders. Our SAB members will be instrumental in providing valuable input toward the further development of the company's regenerative therapies, across Alzheimer's disease, Fragile X syndrome, and multiple sclerosis.

Each of these distinguished leaders in Alzheimer's research bring pioneering expertise and diverse scientific disciplines, including molecular mechanisms of neurodegeneration and regeneration.

Clinical trials of Alzheimer's therapeutics and interacting biochemical pathways of aging, synaptic loss and neuronal loss. Both of our recent announcements are designed and are in preparation for we hope will be positive data, later this year, as we continue to be excited about this trial.

We are fully funded, and when the trial ends later this year, we expect to have over $20 million in cash remaining.

Regarding our initiatives with Fragile X and multiple sclerosis, we are very pleased with the credibility of our partners, Nemours and Cleveland Clinic. We are actively working with both and expect to be in position to initiate trials in 2023.

I now turn the call over to Dr. Alkon, who will speak in greater detail about both these initiatives. Dr. Alkon.

Operator
Please check and see if your line is muted, Doctor.

Daniel Alkon
Sure. Thank you, Alan. Our priority is to develop a drug to cause real and sustained improvement in Alzheimer patients, a drug that will treat the underlying disease and prevent its progression.

Until now, no such drug has been approved by the FDA to cause sustained improvement in Alzheimer patients, as all existing marketed drugs merely slow the debilitating progression of Alzheimer's disease.

We are pursuing this real treatment for Alzheimer's disease with an innovative strategy that has been validated in extensive preclinical models to regenerate and regrow the synaptic connections in the brain and prevent the death of neurons that communicate, through these connections.

We are excited, today, to recap significant recent progress for finding such an Alzheimer's drug and toward optimizing it for practical use in the clinic.

The current dosage has been found to produce clear cognitive improvement, over baseline. As Dr. Tuchman introduced, we expect to announce topline data from our six-month NIH sponsored Phase II placebo-controlled trial for advanced Alzheimer patients in the fourth quarter of this year.

This soon to be completed trial has been optimized through lessons learned from all our previous clinical experience that was recently reported in a peer reviewed placebo-controlled article in *The Journal of Alzheimer's Disease*.

We are continuing this dose optimization process with a just initiated dose escalation trial that will fine tune the dose level called the 20-microgram schedule, to obtain the greatest benefit from the exact dosing levels to be tested.

The purpose of this dosing trial is to prepare for our data expected during the fourth quarter of this year.

Optimizing the lead drug Bryostatin protocol has already uncovered several key steps. These include a rising and an entirely safe protocol. No safety issues nor serious side effects, as approved by our data, safety and monitoring board.

By extending the trial to six months, we expect that the advanced Alzheimer's disease placebo patients will have more than enough time in the absence of treatment, to show cognitive decline as has already been consistently observed for placebo patients, in the past.

Twice the number of doses administered in this extended trial could also offer even greater treatment benefits than was observed with our shorter duration pilot Phase II trials.

Furthermore, to ensure that treatment cohort patients and the blinded placebo patients begin the blinded protocol from the same baselines as current Alzheimer trial has a third-party monitor to guarantee that the treatment of placebo cohorts are balanced. Thus, it is unlikely

that the cohort baseline severe impairment battery values are out of line with each other, as did occur with one of our two pilot Phase II trials.

Eliminating any common baseline therapy with a drug called NAMENDA or Memantine, is now required in our Alzheimer's trials. Memantine has provided transient modest reduction in the rate of patient decline that is not sustained, does not actually prevent disease progression.

Memantine blocks the excitatory glutamate receptor called the NMDA receptor, which is required for synaptic genesis and thus, is required for the synaptic genesis caused by our lead compound, Bryostatin.

In another lesson learned, very severe Alzheimer patients will no longer be included to avoid the inconsistency introduced by very severe Alzheimer's disease.

Synaptogenix is one of the few companies, today, developing drugs to treat the advanced Alzheimer patients now being tested in clinical trials with Bryostatin.

Based on the underlying biochemistry and how Bryostatin appears to work, however, Bryostatin seems to also have potential to treat early and perhaps, even pre-Alzheimer's disease dementia.

The clearly significant treatment benefits, improvement over baseline, and compared to placebo patients of Bryostatin observed in the pilot Phase II trial data that we recently published offer encouragement for clinically meaningful results of our ongoing six-month trial and the dose escalation trial, due to read out, this year.

Lastly, a number of medical centers around the world have started to follow our protocol for Alzheimer's disease and apply it to other kinds of nerve degeneration, with promising results.

We may have, therefore, a leading approach in treating neurodegeneration which today, is based on preclinical data but one we hope will have further clinical applications, in the future.

I'd now like to turn the call back over to Bob. Thank you.

Bob Weinstein
Thank you, Drs. Alkon and Tuchman. We'll take any questions—we'll now take any questions from our investors. Operator, can you please assist with the queue?

Operator
Thank you. If you would like to ask a question, please press "*", "1" on your telephone keypad. A confirmation tone will indicate your line is in the question queue. You may press "*", "2", if you would like to remove your question from the queue. And for participants using speaker equipment, it may be necessary to pick up your handset, before pressing the star keys.

Our first question is from Joanne Lee with Maxim Group. Please proceed.

Joanne Lee
Hi. Thanks for taking the questions. So, for my first question, which you touched on during the call was around the recently initiated optimization trial. Could you just elaborate on the, I guess, the purpose of the study, given that your plan is to evaluate the efficacy of the 20-microgram dose in the ongoing Phase II trial?

Is there a possibility of there being a better dose that could be taken to the Phase III? Thank you.

Daniel Alkon
Well, some—this is Dan Alkon. From our first trial experience, we differentiated between a modest dose, which is the 20-microgram dose, and the higher dose of 40 micrograms.

And that was chosen, based on the known biochemical properties of Bryostatin's effects on synaptogenic growth pathways. However, we also know from the same biochemical information that there are slight differences in very little lowering of the dose or slightly raising the dose.

We didn't check for those because we already had a good, safe dose that was causing improvement, safely. Now, what we're doing anticipating that our data are going to be positive and hopefully exciting, we want to get the very best dose going into the clinic.

So, one, it would not be if we improved that efficacy, the 20-microgram dose but maybe one slightly lower than the 20 or slightly higher, depending on the open label data that we receive.

Joanne Lee
Great, thank you. That was really helpful. And just as a follow-up, I guess, what is the need for dose optimization trial or is it just for the potential readout for the Phase II coming out later this year, the readout?

Is it possible that any signs of efficacy in the Phase II could actually be understating the efficacy if the better or more optimal dose level is discovered?

Daniel Alkon
Well, it is the first possible, and that's what we're checking it for. I think if we have the level of positive results that we're hoping for and excited about, we may not need to have any dose optimization.

But we're being prepared. We're trying to make sure that we're honing in on exactly the best dose to go into the clinic with and to do our registration trial.

Joanne Lee
Great, thank you so much, again, for taking the question. And congrats on the progress.

Operator
Our next question is from Jason McCarthy with Maxim Group. Please proceed.

Jason McCarthy
Hi, can you hear me? Sorry, I had a tough connection.

Operator
Yes.

Jason McCarthy
Oh, good. Okay, can you talk, Alan or Dan, a little bit about the differences between being in mildly severe versus basically every other drug in development being in almost all completely is used to the mild side and what that difference is going to be, in terms of what clinical benefit do you see from a new drug, like Bryostatin?

Alan Tuchman
Okay, let me. Yeah, I'm going to take a try at this and then Dan, if you want to chime in with some more, it's fine.

Jason, clinically, you see a lot of people with early Alzheimer's. And there are drugs that are approved for them.

We don't do anything for people with more severe dementias of any kind, certainly, not Alzheimer's.

So, clinically, if a patient comes to me as a practicing neurologist and sees this particular presentation, we're trying to affect a change. And this would be a major breakthrough because nobody has really gotten any of these patients better.

So, I mean, this is a tremendous need, and nobody has approached it.

Daniel Alkon
I could add a little bit to Alan's answer. I think that, over the last 20 years, the failure of the drugs to actually produce real improvement in Alzheimer patients has caused the industry to move earlier and earlier to the point where it's so early and maybe even early dementia, even before we know that it's Alzheimer's disease, that it may not even be Alzheimer's disease that the drugs are trying to treat.

There's an advantage to that because you're catching the disease early, and we think Bryostatin, by everything it does, pre-clinically and biochemically, can do that, too.

But the problem is that when you get into a more advanced case, it doesn't work. And that's what's happened in the last 20 years.

We purposely took on the challenge of trying to treat advanced Alzheimer's, which means moderately severe to severe patients, which can be quantified because if we thought that we could improve those patients, we'd be doing something for the patient population that, virtually, no other drug has done.

And at the same time, we would not have ruled out the possibility of going earlier, as well. There's no reason why we couldn't go earlier. So, we took on this challenge because we think it's basically a neglected niche and given the suffering of Alzheimer patients, the need is so great that we thought this would be our first target.

Jason McCarthy
Got it. No, that's very helpful. Our view is Alzheimer's should be being treated like a deadly disease like that it is, kind of like oncology, and oncology starts towards the end of the road, so to speak, and then works its way backwards. And that's very true success.

Just whatever interested in the Synaptogenix story. One more question, very broad. And I don't know if you're going to have the answer, until you get the data. But what is the outcome of the Phase IIB--it's a six-month primary, in terms of timing for a durable effect or any effect in this type of patient population?

Because you see the other trials go out 18 months. And six is always debate about how long do these trials really need to be. And then, I would imagine it's going to be different in moderately severe to severe patients.

Alan Tuchman
Well, Jason, I think first of all, we are monitoring these patients, up to 42 weeks. So, we want to see after six months of drug, how long the effect lasts.

Obviously, if we get a positive study, the next study is going to be continuing working on that floor that we've developed and then going forward.

Some Alzheimer's trials go for a very long time but, of course, if you get a significant result, you don't need that to get a difference. So, that's what we're hoping for.

Daniel Alkon
One thing we can refer to, Alan and the questioner, is what we've already seen. We've already seen with even a limited trial, a pilot trial which is only 11 weeks of dosing and 13 weeks of

monitoring, that the improvement we got in patients who were not on Memantine lasted at least 30 days after all treatment had stopped.

So, it was a persistent benefit. So, even our pilot studies indicate that there could be very long-lasting benefits that outlast the treatment effects.

And this is, of course, something that everyone needs and what we want. And we're looking for it in this particular trial and, as Alan said, even going out even well beyond the six months, there's no magic number-six months, eight months.

But you do have to look at the literature. And in six months, if you look at the literature, patients who are advanced in Alzheimer's disease, invariably, without treatment, declined. You can look at the literature and it shows that.

So, that's a guide to us. We want to go out to, at least, six months because we want to see the patients who are declining in comparison to without treatment to patients who we hope are improving with treatment.

And that's what determined it. But we are going out well beyond because we're looking at something--again, this is something that hasn't been done in the industry is to actually observe the persistence of the benefit, long after the treatment has stopped.

Jason McCarthy
Got it. And the last question is, is there potential for continued NIH support are non-dilutive funding from other sources to move into a later stage trial, after the 2B reads out?

Daniel Akron
We're certainly looking for that, and we're certainly going after that.

Jason McCarthy
Got it, great. Thank you, fellows, for taking the questions.

Operator
Our next question is from Chin Lyn (PH) with Lyn Asset Management. Please proceed.

Chin Lyn
Hi. Thank you for taking my questions. Congratulations with the trial. As a shareholder, I'm very pleased that your data is going to be read out on time in the fourth quarter.

Just curious, have you seen the recent signs, article last week basically talking about the amyloid beta, the experiment was fake, the paper is a serious problem. It's another company called Cassava and potentially even has impact with the FDA approved drug. I don't know if you have any—

Daniel Akron
--Yeah, Alan, I can take that question.

Alan Tuchman
Please.

Daniel Akron
I have read that article and actually I was quoted in the article that you mentioned in *Science,* by the writer.

I thought it was a very careful and thorough doc job. It points up something that, whether or not fraud is involved, that has long become apparent, and that is just treating amyloid intel is not likely to really cure this disease.

That result was actually obtained even back in 2008, when Pfizer and J&J and others--an antibody like biotin antibody, they treated the patients, and the patients did not get better. And a scientist named Holmes published an article in Lancet obtaining those results of the autopsy, and he found, in fact, all the amyloid was eliminated from those patients. But it had no clinical benefit.

Now, what I think is worth emphasizing is, yes, our focus is on regeneration-regenerating the synapses and rejuvenating the neurons, revitalizing the neurons. But in addition, Bryostatin, through other pathways that it activates, also reduces amyloid intel.

So, it is multi-modal and its efficacies. It not only is an antigenic and anti-death of the neurons, but it also is anti-amyloid and anti-tel. So, this is another reason why we think that we're covering the bases to try to get this to come home.

Chin Lyn
Thank you, thank you for that. So, do you think the whole pharmaceutical industry was misled by this, potentially, fabricated paper to the wrong direction and now they have a wake-up call that's maybe like approach like you can be the right one?

Daniel Alkon
Well, my own feeling is that the industry has had many reasons to go after amyloid intel, including the fact that my home institute, NIH, Neurologic Institute, defines Alzheimer's disease by gold standard criteria that require dementia in light and amyloid intel and autopsies.

Those are the requirements for identifying a patient, unequivocally, for having Alzheimer's disease. And for that reason, many people, many pharma efforts have focused on dealing with the amyloid mentality. That seems to be part of the definition.

However, I think whether or not the issue is fraud, it's becoming more clear that much more is going on than just having the pathologic red flags of amyloid intel, particularly, the loss of the synapses.

There have been five or six major studies, beginning with Bob Terry in University of California, San Diego, continued with Paul Coleman at Rochester and Don Price and Hopkins, studies where they actually measured synaptic numbers in autopsy samples.

And then they correlated with the cause in deficits. They were closely correlated. Synaptic loss is closely correlated with cognitive loss. However, it's not closely correlated with amyloid intel.

So, whether or not the fraud issue is there, just looking at the data that had been acquired in the pathology studies that I mentioned should have, already, been a wake-up call that we needed to do more than just simply address the amyloid intel.

Chin Lyn
Okay, thank you. Thank you for the detailed explanation. I really hope you're successful. The human race is counting on scientists like you to make advance for this deadly disease.

And also, I'd just like to follow up a little bit. I think the other analyst mentioned that, if you have some indications, you know, fingers crossed in Q4, you have a very good or decent beta, what's your plan?

Do you plan to develop, to do a Phase III trial? I think you have a dose optimization. Maybe that—maybe possibly for that preparation for that, or are you planning to do it on your own? Can you—

Daniel Alkon
--I think that's going to have to come with our results and with the close discussion with the FDA, in close collaboration with the FDA, those decisions will be made as to how we follow up what kind of registration trial.

As far as partnerships with business decisions and those two will probably emerge, as the data are recorded.

Chin Lyn
Okay, great. Thank you and good luck.

Operator
Our next question is from Tucker Anderson with Above All Advisors. Please proceed.

Tucker Anderson

Good afternoon. Nice to meet you, Dr. Tuchman. I know the other two people on the call from previous conversations. And thank you very much for holding this call. And I hope this will be the first of regularly updated to shareholders.

I'd also like to congratulate you on the reconstitution of your scientific advisory board. I think you have a fantastic group of people now, and I would assume they would be very helpful to you.

My first question is in talking about other uses of Bryostatin, in the past, the company has mentioned Parkinson's. And I noticed you didn't mention Parkinson's. Is that just because there's nothing currently in the works, or is there some reason why that was left out?

Alan Tuchman
Either way. Parkinson's, there is good preclinical data from many different indications. We are limited as to the number of ones we can bring into the clinic at a single time.

So, these are the ones we're started with. Do we think Parkinson's is a good indication? The answer is absolutely yes. And hopefully, we'll get there.

Tucker Anderson
Good, that's what I wanted to hear. It's personal with me because of a good friend.

Daniel Alkon
So, just to add to what Alan said, what has emerged--and this is something that we could not have anticipated--is in the last three or four years, other institutions around the world have used their own preclinical models for different types of neurodegeneration and, amazingly, using the same protocol that we've developed, they've obtained very good results, very promising results in this preclinical studies.

And they are even more than we've been able to announce. So, what is emerging is the potential for a general approach to neurodegeneration, a regenerative approach that may have benefit for a variety of neurologic diseases that cause degeneration: multiple sclerosis, Parkinson's disease, Fragile X, ALS, a whole list of them.

It is quite remarkable, but it suggests that neurodegeneration has a lot in common, independent of the way it's caused in these various disease entities.

Tucker Anderson
And I thank you for your foresight, Dan, in understanding that and being a long-term advocate of that possibility because it really could be very exciting.

If you mentioned, I didn't hear it. Have you said how many total enrollees there are in the blinded study, and are they evenly split between placebo and getting Bryostatin?

Alan Tuchman
We haven't broken the blind. So, I can't tell you that people who were entered into the study were evenly split between drug and placebo.

Some patients were early termination. So, they didn't complete the study. We have no idea of the people remaining in the study or have completed the study, which are placebo, and which received drug.

Tucker Anderson
What was the initial total enrollment?

Alan Tuchman
Our goal was to enroll 100 patients.

Tucker Anderson
Okay, thank you.

Daniel Alkon
And the design was for an evenly distributed between placebo and treatment. We are probably going to come close to that. But as Alan said, until we see the unblinded results, we don't know.

And whether or not there are early terminators, they still will be included, once they start into the trial.

So, the likelihood is we'll come to a very close even distribution between placebo and treatment.

Tucker Anderson
Fantastic. And I want to ask, do you have any speculation on how the issues raised by the science article, which I thought was fascinating and I saw not only where you were quoted, Dan, but one of your scientific advisory boards was quoted, well.

Do you have any thoughts on how that might affect NIH funding for current proposals and future proposals, after these sort of questions have been raised? Is it likely to have any affect? Is it likely to put everything on hold, or what would you see happening?

Dan Alkon
Well, having served on those study sections, I know that it's a slow process of changing the accepted wisdom.

And while this particular example of misapplied information about oligomers, which are the salable form of amyloid before it becomes plaque, will have some impact.

My gut feeling is that it'll be a slow change. We're talking about a paradigm shift, whether or not it's our paradigm, which we hope it is, a regenerative paradigm that we're developing, or it's another paradigm.

Shifting a paradigm takes time, and it takes a lot of evidence. So, I don't think it's going to happen with one important article, which this was.

Tucker Anderson
Yeah-no, it does—I agree, totally. And it does take time, and it does take a lot of evidence. But the way cognitive dissidence works is, once it happens, it happens all at once.

And people sort of, when they do a flip after a long period of inaction, they suddenly, all at once, say, oh yeah, I was wrong, and the other way was right, as somebody who is a student if cognitiveness is.

I thank you guys very much for holding this call. And as you know, I wish you great luck.

Alan Tuchman
Thank you.

Operator
Our next question is from George Mal (PH), private investor. Please proceed. We lost George's line. So, our next question will be from Tom Bishop with BI Research. Please proceed.

Tom Bishop
Hi. I've got a question on the dosing trial. What doses do you plan to study, and how many patients do you expect, and what is the timeline in that regard? What does that do to the start of Phase III?

Daniel Alkon
I don't think it's going to affect our Phase III. It may help us fine tune it, but it won't. And the doses that we're looking at are a significant reduction from the 20 micrograms of about 30% and a significant dosing level and significant increase of about 30%, something like that.

And we'll see if those changes, those increments, make any difference for, again, fine tuning what we hope to do a registration Phase III trial with.

And the patient numbers are small, but they are going to be sufficient to get interpretable results, we believe.

Tom Bishop

In terms of the Phase III, I didn't mean the protocol but the start of the Phase III trial because I didn't know quite how long this will last to be able to determine the—

Daniel Alkon
--It won't, in any way--it won't in any way impact on our timeline for Phase III. But the real determinant will be our readout, our topline data of our six-month trial.

And by the way, I would say that readout, in my opinion, is going to have the potential, if it's good, of having an impact on paradigm shifts, much more than reports on occasional fraudulent data.

Tom Bishop
Yeah, great. A number of--you mentioned that a number of hospitals are following our protocol. I was interested to hear a little bit more about that. In what regard?

Daniel Alkon
Well, they virtually have used the same preclinical protocol that we published. So, for example, Johns Hopkins used our protocol and our *Journal of Neuroscience* article. They used that protocol in a multiple sclerosis preclinical trial, got terrific results.

And it's not surprising because multiple sclerosis, at the onset, involves synaptic growth factors. The synaptic growth factor deficiencies is what causes the demyelination and, potentially, when they are restored, the synaptic growth factors can cause remyelination.

Now, the Fragile X trial, we did at the Rockefeller Institute, and we got what we thought were very promising preclinical data. And then, the Alzheimer's--the Fragile X foundation, headed by Mike Tranfaglia, collaborated with us on a third replication, all of which, again, were in agreement and which generated an orphan drug status for Fragile X, before our current trial.

But other centers have, for example, worked on Parkinson's disease and published articles on it. The final pathways are always a little different, depending on the disease. But they all seem to have in common certain aspects of degeneration that our drug modality seems to be addressing.

Tom Bishop
So, when you say that they're following your protocol, you mean the synaptic regeneration concept? Is that what you mean by—

Daniel Alkon
I mean, using Bryostatin in the doses and in the frequency that we've already published.

Tom Bishop
In other words--

Daniel Alkon
-- It's exactly our drug and often same frequency duration that we published in our own preclinical studies.

Tom Bishop
Okay, good. And with regards to Fragile X—

Daniel Alkon
--It's kind of a duplication with a different disease model. And that's what's so exciting because all these different disease models have different ideologies, different causes. But the consequences seem to be so much in common with the Bryostatin in the same dosing and the frequency levels that we use ourselves, seems to have great benefits for these different disease models.

Tom Bishop
Okay, good. That's interesting. And the Fragile X Nemours DuPont announcement, that was almost a year ago. I'm just wondering what's the holdup there and so what—

Daniel Alkon
--It takes time.

Tom Bishop
--Well, the first—

Alan Tuchman
-- Let me give him a little detail. Before we can start in Fragile X, in neurologic diseases, unlike oncology, we need a new IND for each indication.

So, we have been working, gathering the data to submit to the FDA for a new IND for Fragile X, which is almost ready, will be shortly submitted and, hopefully, accepted.

Then we can go on and do a study. Prior to that, we cannot.

Daniel Alkon
The same thing is true for multiple sclerosis. We've been working very intensely and collaboratively with the Cleveland Clinic. Superb MS personnel and staff. We've been developing a protocol to go for an IND for multiple sclerosis, as well.

Again, dotting the I's and crossing the T's to make a successful submission to both, IRB and FDA deliberative bodies.

Tom Bishop

Okay, is it a good assumption that the Fragile X will be out of the gate first, therefore?

Daniel Alkon
I think we shouldn't speculate about that. We don't know.

Tom Bishop
Okay.

Daniel Alkon
Hopefully, they'll both be out soon.

Tom Bishop
You mentioned that some dropped out of the phase, the most, the ongoing trial. And I'm just wondering, did you enroll in excess of 100 to allow for that, or are you just—

Daniel Alkon
--We enrolled enough to anticipate the experience that almost all Alzheimer's trials have, which is a 25% to 30% drop out, before completion.

So, we enrolled enough patients to have a significant cohort placebo, significant cohort treatment. So, we anticipated that. And that was also anticipated in our submission and our approval of the NIH grant that went along with it.

Tom Bishop
Well, does that mean you enrolled more than 100 or you just, it was—

Daniel Alkon
--Yeah, it does mean that. We did enroll more than 100.

Tom Bishop
Alright, great. Alright, well, thank you.

Operator
Our next question is from Larry Stoffman with LDS. Please proceed.

Larry Stoffman
Hi, thanks for this. And congratulations on the work that you've done, to date, and on the new scientific advisory board. It's a very impressive group.

I had a couple of questions about the compound, itself. The first thing, it's very difficult to obtain the natural product from the marine organism, and there is a synthetic version that you have helped to work on.

Is there any thought—is the synthetic version installed in any of this work, to date, or is there any plan of using the synthetic version either for treatment of advanced AD or for the other neurological disorders, like Fragile X?

Daniel Alkon
Alan, why don't you field that one.

Alan Tuchman
All of our studies, to date, have been with the natural product. The synthetic product, which has been licensed from Stanford, has been manufactured as an API, and we hope to be involving it, using it in future studies.

But there are a whole bunch of hoops that we have to jump through to show that this is the same drug and that we can use it, equivalently.

Daniel Alkon
So, we'd have to establish, and we are establishing what's called bioequivalence of the synthetic form, which we have every reason to believe will be established.

We do have an exclusive license with Stanford for the synthetic for all neurologic indications. We are constantly working with Stanford to make sure that both parties are in agreement and we're fulfilling their expectations and our expectations.

We have in our possession a full gram of synthetic compound, which is what we're using for bioequivalence. So, we are ready have shipment enough to actually supply many patients with it, once we have established the necessary framework that it's bioequivalent, which we are optimistic it will be.

So, we're setting ourselves up to have a synthetic line of supply, indefinitely, for the future. We're trying to get there. We're very optimistic that we will. And it's a tremendous breakthrough that we have benefited from because, as you probably know, the natural compound, at first, was harvested from 18 tons of bryozoan and at the cost of hundreds of millions of dollars.

The National Cancer Institute gave us, as virtually the only grantee of that, a source of that natural compound for all the trials that we're doing right now, but we're moving toward the synthetic, as I mentioned.

Larry Stoffman
So, you would anticipate for a follow-up to Phase II and a Phase III clinical setting either using the natural product again or, if possible, the synthetic.

Daniel Alkon

Yeah, we can't say, at this moment, which one we'll use for the Phase III. But ultimately, we're essentially establishing a line of supply that should just go into university general use, across the country and maybe across the world, we'll have a synthetic supply.

Larry Stoffman
Right. I'd imagine that would also be of interest to others in the field, other pharmaceutical companies as well because I assume Stanford has patented the synthetic.

Daniel Alkon
Well, yeah. It's patented. But again, that's part of our license agreement. Through that patent, we have exclusive access to it for all neurologic psychiatric indications.

So, it's important from the point of view of supply but also from the point of view of proprietary patent protection.

Larry Stoffman
Right, so, the cost there, if this was successful drug intervention of using the natural compound would probably be prohibited, going forward. I mean—

Daniel Alkon
--No, we don't intend to ever do that. We've been very fortunate to have as much natural compound as we need to do all these trials but going into the clinic commercially, we intend that that will be synthetic and be available.

Larry Stoffman
Thank you. One last question. There's been a lot of work done on some of the biochemical pathways with respect to AD and other compounds that are in trial.

In some talk recently, I read about air and toxicity and the role of Bryostatin one and gathering that up from the process insulating. Do you see, going forward, the possibility that if in a successful treatment regime you're not going to be ever using one drug say, based on Bryostatin but a combination of compounds—

Daniel Alkon
Yeah, I think that's possible. But we don't know yet because it is multimodal. It has multiple effects, not only synaptogenic but also reducing amyloid intel.

The good news is that we already know, from our past experience, from the published results, that the Bryostatin one that we're using is amazingly safe. It doesn't have any mysterious adverse events associated with it.

So, we're delighted, and that has continued to be true, even for the ongoing trial, right now, that it has been safe. So, we're essentially doing no harm and, hopefully, we're going to do a lot of good.

Larry Stoffman
Thanks very much. Thank you.

Operator
Our next question is from Tincravi Iliana (PH), a private investor. Please proceed.

Tincravi Iliana
So, thank you for taking my question. I wanted to ask about the synthetic compound, too. So, my question is, at this point, what is the timeline to get into the synthetic compound?

Daniel Alkon
Well, as I mentioned, we already have the synthetic compound in our possession, a gram of it, which can actually treat an amazing number of patients. And we're just starting to--

Tincravi Iliana
--So, to get to the proof of bioequivalence.

Daniel Alkon
Alan, why don't you address that?

Alan Tuchman
We have to do two things. We have to do--prove bioequivalence and then we have to take the API, the active pharmaceutical ingredient, and make it into a drug. It has to be put into a powder that can be lyophilized and then infused.

So, we will have announcements, along the way, as we meet each particular stage. But it is a relatively short-term problem and will not interfere with the timeline of our studies.

Tincravi Iliana
Thank you. Got it. Good luck with the whole studies.

Daniel Alkon
Thank you. Operator.

Operator
Our next question is from Robert Smith with The Center for Performance Investing. Please proceed.

Robert Smith

Good afternoon. Thanks for taking my question. I hear some music in the background.

So, yeah, let me speak to your tenacity. First of all, I assume that you feel the trial is sufficiently powered as it's been telling.

Daniel Alkon
It's hard to hear what you just said. Could you repeat that?

Robert Smith
I assume that you feel that the trial is sufficiently powered, how you've done this.

Daniel Alkon
Yes, we do.

Robert Smith
The number of--how many sites are there?

Alan Tuchman
There are 17 sites that are contributing subjects for this trial.

Robert Smith
Are they all domestic?

Alan Tuchman
All domestic, yes.

Robert Smith
Thanks. So, there's been a trend in healthcare from large Pharma and large biotech to partner with earlier stage companies. Has there been any indication whatsoever that, at least what's been out there to date, of any interest by any entity of that kind in your work?

Alan Tuchman
I think it's kind of premature for us to comment about that.

Robert Smith
Okay. Can you share with me, what are your two chief concerns, going forward?

Alan Tuchman
Well, obviously, we're looking for a positive trial. And once that happens, we have to interact with the FDA to get their advice and consent for going forward for the next registration type trial.

Robert Smith

Yeah. Is there any timeline, based upon your knowledge about what that would be and the conclusion?

Alan Tuchman
First of all, we need the data. We're going to have topline data at the end of the fourth quarter. However, the data has to be thoroughly looked at. And then, we have to have an FDA meeting.

The timing of that is really not up to us. So, I don't know how we can add to that.

Daniel Alkon
I would add, though, Alan, that if we get really positive data, it depends on the data so, get data really positive, the FDA may very well facilitate our path.

Alan Tuchman
They very well may. But that is their call, not ours. It's not in our hands.

Daniel Alkon
Right. The other aspect of this question that just arose is that we are fully funded, right now. So, we are not sitting on a knife edge as to whether or not the timing of the FDA response is going to have a big impact on funding.

We are fully funded. And we are going to be considering different ways of going forward, possibly funding ourselves, possibly doing it with a partner, etc. All of those options are going to be considered.

Robert Smith
Yeah, I would assume again that to get really good results, there's no way that the agency would not hop on this, right away, and give you some sort of a ring.

Bob Weinstein
This is Bob. I just wanted to correct one thing. Alan mentioned that the data will be released or available at the end of the fourth quarter. We're not sure when, during the quarter, the data will be available. But we believe it will be available, during the fourth quarter.

Robert Smith
Well, that also includes the year end holiday period. So, are you saying it may not happen in the fourth quarter?

Bob Weinstein
No, what Alan said was it would be at the end of the fourth quarter. I'm just reading in the rating that it will be during the fourth quarter.

We anticipate that it will be available, topline data will be available, during the fourth quarter**.**

Robert Smith
Okay. Thanks so much. Good luck, guys.

Bob Weinstein
Sure.

Daniel Alkon
Thank you.

Operator
Our next question is from Ron Fonbra (PH) with Richland. Please proceed.

Chuck
This is Chuck for Ron. You talked a few minutes ago, or earlier in the call, about if you get a significant result, the trial doesn't need to be that long.

Dr. Alkon, you've had a lot of interviews where you described a patient who really couldn't care for themselves, staring at the wall. And they take Bryostatin and suddenly, they can feed themselves and do basic tasks.

I'm sure you saw the Pizza Hut founder story was just unbelievable. And I was just--two questions on it. One is your own impression of--none of that could be possible. I mean, Alzheimer's patients, by definition, cognitively, probably wouldn't even respond to a placebo because they wouldn't even know they are taking it, per se.

I just wanted to get your view on how these kind of results could be possible, unless it was active and efficacious.

And then secondly, if you could just go back to the Phase IIB, the second trial where you talk about this imbalance. And if you could describe in layman's terms, what an imbalance means in this regard and why that would have had the placebo done better in that case. It would be really helpful to get into the context.

Daniel Alkon
Sure. So, the first question has to do with our compassionate use trials. We did several of those. And those were all advanced patients.

And of course, we did know exactly the right dose. But these patients showed remarkably positive responses. There was no question about it. And considering that they were so advanced, it's hard to imagine, especially because those patients' benefits were sustained. They continued over many weeks and even months for that to be a placebo benefit.

So, I don't think—I think your surmise is right, but it's not very unlikely that those were placebo benefits.

And with respect to the second Phase IIB, what happened, which will not happen in this trial, was that by just chance, random enrollment, by just chance, it happened that the patients who were ultimately fated to get placebo started with higher baseline SIB metrics, severe impairment battery metrics.

They started with higher metrics. And what we described in our last article published a few months ago was that the benefit that the patients can show is, statistically, correlated with where they started.

So, if they started higher because of a baseline imbalance, it could have skewed the results. Fortunately, we had enough patients in the moderate stratum, which I think was two thirds of the patients, where we could restrict our analysis of exploratory analysis to just the moderate stratum.

And that's what we used in that paper for both Phase II trials A&B.

However, in this current trial--and this is very important--we have put in a blinded observer, a third-party observer. We have no impact on that person. But that person can check to see if, by chance, there was a skewing that some patients, either placebo or treatment, or starting at a higher point.

And then, he or she, whoever is doing that work, can then rectify that balance, so that they are evenly distributed.

We learned from the second Phase II trial that we needed to provide for that. And we have. And so, it's very unlikely to happen in the current trial.

Chuck
And just on that—thank you for explaining that--the idea sounds like that person had a better score to start with, therefore, when you're comparing that with zero, it looked better and that's random.

But wouldn't they have been compared to their own baseline and that would get rid of that effect?

Daniel Alkon
That helps, but it doesn't eliminate it, entirely. And for making a consolidated analysis on both Phase II trials, we just simply used only patients who were in the moderate stratum. In that case, the baseline SIB, the baseline that they started from was very comparable for both treatment and placebo, in both Phase II trials.

Chuck
Thanks so much, guys, and good luck.

Operator
Our next question is from Jack Mayer (PH), Private Investor. Please proceed.

Jack Mayer
Good afternoon. Thanks very much for taking the call. And congratulations and best wishes.

You mentioned that there are others who are using this same free clinical model. And if I understood you correctly, they're also using Bryostatin.

Could you comment a bit on your IP position with respect to using Bryostatin for neurodegenerative degenerative diseases?

Daniel Alkon
Well, we're not the experts on this. But we have invested a lot of time and money to make sure that our IP positions are covered.

First of all, we have use patents coverage for Bryostatin, itself. And in each of these different indications, we have filed for patent coverage, as well.

In addition, we have developed what we think are proprietary protocol dosing. And that's not just the drug but it's what the level of the drug and how frequently you give it. And that is also proprietary, and we have patent coverage for that, as well.

Some of those are issued. Some of those are filed. But we have a fairly extensive patent portfolio coverage for many different diseases, including some of these other indications that other institutions are working on.

Alan Tuchman
And in addition, we have the exclusive license for all central nervous system diseases for the synthetic.

Jack Mayer
Okay, thanks very much for explaining that. Now, in terms of timing, this dose optimization trial, you expect that to read out concurrent with the current phase trial or at some other time-Phase II trial?

Dan Alkon

We don't know exactly, but the timing of that, we can't give you an exact timing on that. But we don't, in any way, expect that dose escalation trial data to slow down our timeline toward registration, if our results for the six-month trial are positive.

Jack Mayer
Okay. I was looking for that trial in the clinicaltrial.gov site and could not find it. Is that a trial that you would normally need to put there, or is there some reason why it wouldn't go there?

Daniel Alkon
I don't know the answer to that.

Alan Tuchman
Are you talking about the dose optimization trial?

Jack Mayer
Correct. The other one is very clearly there.

Alan Tuchman
Right. That would normally, it is not a randomized. It's an open label trial. So, it normally would not go in that site.

Jack Mayer
Got it. Okay. Excellent. And then, in terms of bioequivalency, leaving aside whether it would or wouldn't interfere with your getting started with the registration trial, just looking at it separately, how much time does it take something like that to get done? How long should it take to get something like that done?

Alan Tuchman
Bioequivalency is a relatively quick study and should be done, shortly, sometime in the near future. Making it into a drug requires a manufacturer. And that's something we are looking at, actively.

Jack Mayer
Would it be unreasonable to think that you can get bioequivalency done, this year?

Alan Tuchman
It would not be unreasonable to think that.

Jack Mayer
Okay. Now, in terms of a manufacturer, can you give us some sense of how long that sort of thing would take?

Alan Tuchman

We're talking about—

Jack Mayer
--Some Sense.

Alan Tuchman
Some sense, okay. There are long waits to get manufacturing done, whether because of COVID or COVID being used as an excuse. But lots of things have been slowed down. It should take months, not years.

But I can't be any more specific than that.

Daniel Alkon
But we can also say that we're not going to rule out using the natural substance for the next trial, just assuming using the natural source of this.

Alan Tuchman
Yeah, there will be no delay—

Daniel Alkon
--We can still use the natural substance for the next trial, not only from our own stockpile but also from the NCI. So, we don't want to rule that out and confine ourselves only to using synthetic.

We can and we tried but we're not ruling out the natural.

Jack Mayer
If I could perhaps rephrase what you said, and correct me if I am mistaken, if you need to, you have access to sufficient natural supply to do a registrational trial, if you've shown bioequivalency, and that has nothing to do with manufacturing.

Then if you are successful with a registrational trial with the natural substance, you can automatically use the synthetic substance, if you've established bioequivalency.

And then somewhere along the way, deal with manufacturing and if manufacturing is delayed, it's delayed. But between those two, you can finish your trial.

Daniel Alkon
That is my understanding-yes.

Alan Tuchman
I think that's reasonable.

Jack Mayer
Okay. The clarification is much appreciated, and wish you all the best, gentlemen.

Daniel Alkon
Thank you.

Operator
Our next question is from John Bowden, Private Investor. Please proceed.

John Bowden
Good afternoon. I was just wondering if I could get some thoughts on some of the more recent research that's come out, one that shows that Bryostatin could, potentially, help modulate the iron, as far as relating to the AD pathology.

And also, if you could comment on the research that came out about the vascular endothelial growth that you press released a few months ago.

Does that have possible repercussions, even beyond Alzheimer's, possibly other forms of dementia?

Daniel Alkon
Absolutely. They're both-- vascular endothelial growth factor is very important, also relating to oxidative stress, which is often a factor of neurodegeneration. The fact that Bryostatin reduces oxidative stress and increases the vasculature available is beneficial.

And it's beneficial, not only for Alzheimer patients but for other forms of neurodegeneration. It increases the general potential of the drug and drugs like it that we have in our platform.

But in addition, you asked a different question. Maybe you could repeat that part of it.

John Bowden
Yeah, there's been some more research on iron like disk homeostasis and its effects on the AD pathology and that Bryostatin could possibly help modulate some of those issues.

Daniel Alkon
Well, I don't know about that particular target, but what I do know is that when we did a lot of this work in preclinical studies at the Rockefeller Institute where we showed that Bryostatin via its major target, PKC Epsilon, activates all three of the natural major degrading enzymes for A Beta. And A Beta oligomers.

So, the natural degrading enzymes, one of them is called Neomycin. Another one is insulin degrading enzyme. Another is ECU. They're all activated by Bryostatin. So, it's naturally activating via its major target, the degradation of A Beta oligomers.

You don't need anybody to just reducing the amount of A Beta Oligomers. In addition, it also blocks the phosphorylation of TAL, which produces the neurofibrillary tangles.

So, it blocks the formation of the other major pathologic hallmark by again, its PKC epsilon pathway. These are not the only other major effects that we see, we're looking at synaptogenic effects.

But the natural steps in the brain for degrading A Beta oligomers and for preventing the formation of neurofibrillary tangles are both activated by Bryostatin.

John Bowden
All right, and one last question, if I could. I know, and there's been some new research showing that there's an imaging technique that might could possibly measure the number of synapses in the brain.

And I was wondering, is that something that is years away to possibly use as a biomarker? Is that something that's—

Daniel Alkon
--It's a great question. I'm certainly aware of—we're aware of programs that are being directed toward that.

In my opinion, although those programs have made good progress, none of them have succeeded at the resolution of individual synapses. What they measure are virtually large areas of synapses. So, you can see if you have a large area, or maybe hundreds of thousands of synapses knocked out. Then that will show up with those methods.

So far, the methods have not reached a resolution where we can look at individual synapses. However, and this is the way we helped validate Bryostatin, an autopsy, and autopsy brains, you can measure the number of synapses.

And that's how we quantify that brass down PKC epsilon BDNF growth pathway to actually restore the number of synapses and close association restoring cognition.

And in the human brain, autopsy studies, the number of synapses is closely related—that's again, at autopsy, not in vivo because your question really is in vivo. But in autopsy, you can measure them, and you can show that relationship of cognitive benefit to synaptic number.

The technology for doing that, in vivo, has not been realized yet. But it will be, I'm sure, in future years.

John Bowden

All right, thanks for the response.

Operator
And now our final question is from Mason Holt, Private Investor. Please proceed.

Mason Holt
Hi. In 2019, your predecessor company, Neurotrope, ran a Phase II trial, which failed.

What's the difference between that trial and the one you're conducting, right now?

Dan Alkon
The trial failure was to reach the primary end point that was defined a priori, before the trial began.

And that's because we had not the knowledge, the foreknowledge, of certain lessons learned, such as the fact that you can have Memantine or Namenda when you're treating these patients because it blocks the effect of Bryostatin.

This is one of the things that we learned. That's one of the major differences.

But there are other differences, too. So, for example, this trial is running at least six months. So, it's double the number of doses that the patients are getting, giving more possible room for efficacy but also, it gives much more opportunity for the placebo patients to go through their natural decline, which all literature says that they do.

When you have advanced patients, these patients don't get better; they decline.

In our previous Phase II trials, which you referenced to in 2019, the trial was half the length of the present trial. Fortunately, we learned that we have to increase that length, which is much more consistent with what the industry has used for looking at other drug candidates.

Mason Holt
So then, why did you have to do a merger with McCutcheon Pharmaceuticals to get to one you could carry-on?

Daniel Alkon
I think you're asking a business question, and I don't think that's something that either Alan or I can quite answer. There's not a forum for that kind of question

Mason Holt
Okay, one last question. How much money have you got in grants from the NIH?

Daniel Alkon

Well, in the current trial, we have a $2.74 million grant that we have spun out. The amount of money that we got from the NCI in lieu of the drug and giving the grant is worth tens of millions of dollars because that kind of natural drug is just not available, unless it was granted to us by the NCI.

And we were presenting in front of a committee of the NCI. They made the decision to basically provide us all the drug that we needed for all the trials that we're doing, right now.

And that is worth tens of millions of dollars. I would say, $30 million-$40 million.

In addition, we had other grants at the Rockefeller Institute who we had a relationship with, which also represented billions of dollars.

So, you have to really consider all these different pots of money, if you really want to add up how much money that we use. But I think it's more appropriate to look at the whole history of the research that was done to reach the Bryostatin.

The Rockefeller Institute, we estimated that there was about $100 million that was made available. At the NIH, it was, at least, $100 million from that program.

And all that research was fundamental framework research that made it possible to generate a drug platform, which is what we have, today.

Mason Holt
But Blanchette Rockefeller never gave you any money, directly?

Daniel Alkon
What was that? I'm sorry. What was that?

Mason Holt
If I'm correct, Bryostatin came out of Blanchette Rockefeller. Is that correct, or not?

Daniel Alkon
It came out of the research that we were doing at the Rockefeller Institute and at the NIH. There were many building blocks and stepping stones. To reach, actually, the drug to be used in clinical trials, that, more or less, had started directed funding when we spun off a for profit entity from the Rockefeller Institute, which was called Neurotrope, at that time.

And then, money started to be generated, basically, as a process for drug development from industry and investor sources.

Mason Holt
Okay, so—

Daniel Alkon
But to do that research, to reach that, to even test Bryostatin, for example, and transgenic Alzheimer's models and Fragile X models, to do that work required a huge amount of support that did come from the Rockefeller Institute.

Bob Weinstein
Okay, well, that was our last question. And thank you for the question. And we're going to end this call, at this time.

Thank you, all, for participating.

Operator
Thank you. This does conclude today's call. You may disconnect your lines, at this time, and thank you for your participation.