



November 17, 2024, Monthly Update

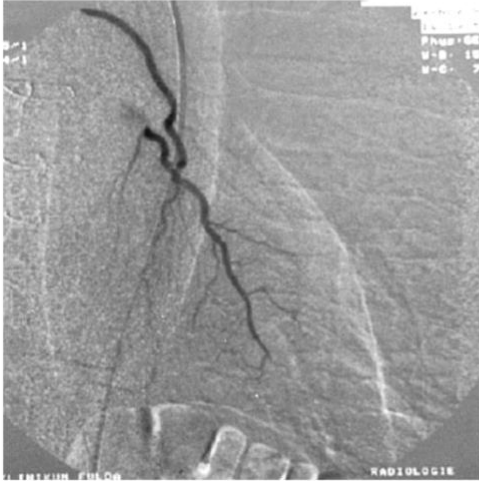
The Brain Healing Process — Parkinson's Disease.

Our medicine, FGF-1, was first discovered in the mid-1980s. Over the last 40 years, thousands of medical researchers have conducted studies on using FGF-1 in animal and human research studies to attempt to understand how and why it causes the human body to heal itself. Zhittya has access to thousands of research studies and papers written by others which have accelerated our understanding of FGF-1 healing the heart, brain, legs, diabetes and more. The data on FGF-1 indicates a more robust biological response occurs when the surface receptors for FGF-1 on stressed cells have effectively been able to reset (upregulate) after a prior FGF-1 dosing. We have seen in the heart, a one-time injection of FGF-1 into the ischemic areas of the heart muscle triggers the growth of a new field of blood vessels, thereby providing new blood flow to starving heart muscle. Here is a picture published in the American Heart Association's, peer reviewed journal "Circulation" on FGF-1 growing blood vessels in an ischemic heart.

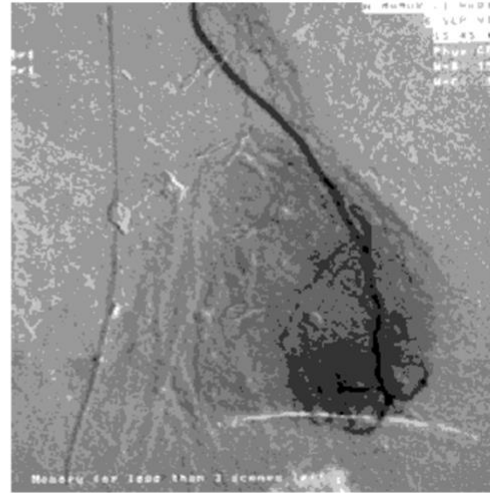
A coronary angiogram in a patient with severe CAD before and 12 weeks after the

local administration of human FGF-1 into the ischemic heart wall. A “blush” of new blood vessels can be seen around the site of FGF-1 administration.

CONTROL



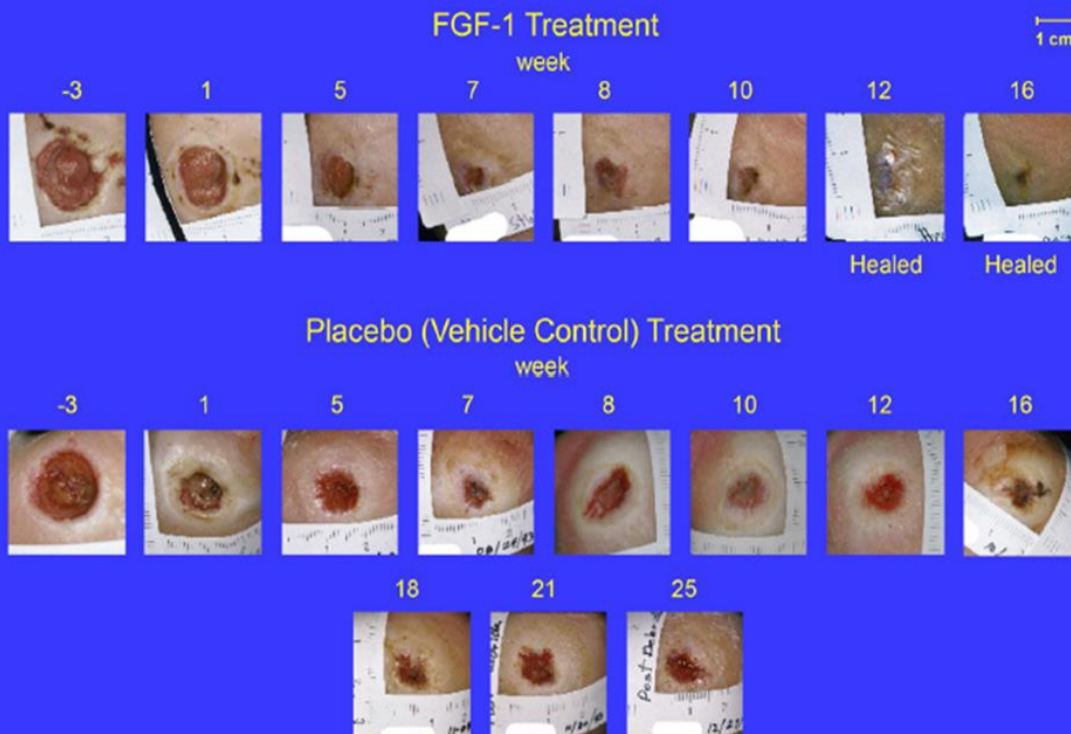
FGF-1 TREATED



We have seen that the same FGF-1 molecule can heal a large chronic diabetic foot ulcer, by dosing FGF-1 (every other day) over a period of 4 to 6 months. Below is a picture of FGF-1 dosed and a placebo treated diabetic foot ulcer. You can see from week 1 to week 16 that the wound continues to heal, and the skin regrows and closes the wound over 12 to 16 weeks. A onetime dosing of FGF-1 does not provide enough healing to close this type of wound.

I believe in the brain we have learned now that we need more dosing, over a longer time frame, to heal the brain's vascular dysfunction and other more complex activities, such as neurogenesis, which enhances the person's own natural stem cell regeneration.

Phase IIb Healing Examples



I show these two examples to address the natural healing process of different parts of the body. With the heart, one round of FGF-1 injections and the treatment is completed. Diabetic foot ulcers require repeat dosing over months to close a non-healing diabetic foot ulcer wound.

For healing the brain from Parkinson's disease, we have animal data (monkeys) which shows that with 5 to 7 months of monthly dosing, there was material improvement in motor scores for the treated animals. The delivery of the FGF-1 with the monkeys was by a direct injection into the brain with a needle. We believe that this delivery method is invasive and less desirable than our intranasal

method for delivering FGF-1 into the brain. From the animal work Zhittya conducted with the University of Minnesota, we can see an intranasal delivery of FGF-1 up the nose can transfer large amounts of FGF-1 into the brain (trillions of molecules) without pain or discomfort (no skin is broken). Now, Zhittya has treated almost 200 research subjects with Parkinson's disease who have dosed FGF-1 into their brains. The first people were dosed about 30 months ago at dosing level one. We watched to confirm that the level of FGF-1 dosing was safe, and a few months later we then increased the dosage for the next round of test subjects. One part of our protocol stipulates that any enhanced dosing Zhittya develops is automatically given to each of those test subjects from earlier study cohorts. It is only fair that those who showed us it was safe early in the process have earned the right to get any improvement in the dosing.

We have now been giving the test subjects Protocol 17, which is cumulatively about 40 times more FGF-1 than the first test subjects received. We have seen enhanced improvements as test subjects have received more FGF-1 over a longer period of time. The reason I wish to share this is that many people think that a dosing of FGF-1 in the brain is similar to the one-time injection of FGF-1 into the heart. One dose and done. It is not. It takes months of treatment for FGF-1 to heal a diabetic foot ulcer. People can see the diabetic foot ulcer wound on the surface of their skin, they cannot see the damage to the wound within their brain that is causing Parkinson's disease, dementia, strokes, traumatic brain injuries, and more.

On December 3, Vika and I will be in St. Louis, Missouri at the Washington University School of Medicine for the 6-month follow-up MRI brain blood

perfusion scan of one of our patients. When the data is analyzed, we hope we see an image of enhanced blood flow in his brain after 6 months of FGF-1 dosing. His movement scores have improved, and his memory is better. Why have they improved? I hope that the brain scan will especially show that his improvement is from increased blood flow in his brain caused by FGF-1 dosing.

A football player cannot see the ruptured and damaged blood vessels in their brain from many concussions after playing football for ten years. From the neurological condition of those damaged blood vessels, neurologists can diagnose them as having Parkinson's disease, TBI, CTE or ALS. I believe most neurodegenerative diseases are the result of vascular dysfunction in the brain. Not enough blood getting to where it is needed. If the 6-month scans show enhanced blood flow in the brain, then I believe we have a treatment for many cerebral vascular dysfunctions, such as Parkinson's disease, stroke, Alzheimer's disease, dementia, autism, PTSD, ALS, CTE and many of the over 250,000 TBIs (traumatic brain injuries) that occur every year in the United States. Please read Dr. Jacobs' section on TBI's causing blood vessels in the brain to rupture, causing vascular dysfunction. Yes, there is a natural healing process to repair that. If, however, it is deficient, does that person over time develop Parkinson's disease? Muhammad Ali was diagnosed with Parkinson's disease. Is being "punch drunk" the result of ruptured blood vessels not healing enough? If we had given Muhammad Ali FGF-1 up his nose, could we have reversed his condition that he developed from sports injuries to his head? I think so.

Healing the brain is a slow and very complex process. We can see patients have improved motor scores and brain function. Now, Zhitty needs scientific proof of

why the patients have improved: such as enhanced blood flows in the brain caused by FGF-1.

I believe with the brain scans, hopefully showing enhanced blood flow, we will have that proof. Soon I hope we can prove that FGF-1 can change the lives of the 200 million people suffering from these brain diseases.

Vika Montano's Patients' Comments Section: Every month, I receive emails and phone calls from our test subjects. We receive more emails when people are preparing for the next round of FGF-1 dosing. Here I have selected a few of their comments so you can read what those who have joined our Medical Research Studies are reporting to us.

Dear Vika,

Just got back from the Neurologist office. Good news! She noted how good his movements are, and she asked if we are still using that "nasal thing". I told her we were still dosing with FGF-1 and explained again the process. She said it must be working because his movements are improving. So, we are cutting back on the Carbidopa/Levodopa (which she said causes hallucinations and delusions) each week until he is completely OFF of it! We will watch to make sure his movements are not affected. Joey now seems much more encouraged with the success she has seen. He seems happier. I believe he now sees that there is hope, and he CAN fight it.

I want to thank you so much for your help during the trying time after my hip replacement. The encouragement you gave and the updated FGF-1 and new

protocol, I believe, has been just what he needed. His hallucinations still persist, but the delusions have subsided.

To keep you updated, he is now on xxxxx, xxxxxxx, xxxxxxxx and xxxxxxx.

You, Dan and Dr Jacobs are so wonderful. You don't know how much we appreciate you.

Please keep us in your prayers.

God Bless you all,

Linda

Patient Two:

Remarkable improvements were observed with FGF-1 treatment.

Dear Zhittya team,

I wanted to share an update on my experience since starting the FGF-1 treatment for Parkinson's under the current protocol. I am truly grateful for the strides Zhittya Genesis Medicine has made in this research study, as I've already noticed positive changes in both physical and cognitive symptoms.

The most noticeable improvement has been with my tremors. They have significantly decreased in both frequency and severity, allowing me to regain control over movements I once found challenging. For the first time in a while, I am able to eat with my right hand again, a milestone that brings a renewed sense of independence and confidence. I'm a 4.0 pickleball player and a 10-handicap golfer which amazes all my friends and me sometimes, but it's so much fun :-).

Additionally, my cognitive clarity has improved. I feel that my mind is less “foggy” and I can engage more fully with daily tasks, which has uplifted my quality of life. These developments give me hope and encouragement as I continue the treatment under the updated protocol.

I am excited to continue making progress under this protocol and feel optimistic about what each new phase of treatment may bring.

Thank you for the dedication and research that make these results possible. I am eager to see what the next steps hold.

Warm regards,
Bobby

Patient three is very amazing to me. When Mark and Sue arrived in the British Virgin Islands, he was in a wheelchair and could only walk short distances with a walker. Other health issues have come and gone, and Mark has slowly continued to improve. An email from Sue below, will give you some idea of her happiness in seeing him improve from his Parkinson’s disease – from wheelchair to walking unassisted makes me very proud of Mark. Sue and Mark, we are all praying for his continued improvement. He is setting a wonderful standard, showing that improving from Parkinson’s disease is possible! Vika.

Patient Number Three:

From: Sue

Date: November 9, 2024 at 11:08:19 AM PST

Subject: Accomplishment

Hi Vika

Here is Mark's accomplishment today. He walked one big lap down and up our driveway without any interventions from me. We both got emotional when that happened. He's still recovering function from when he had Covid pneumonia the first part of September.

On Tuesday he will receive his dosing. We're praying for even more recovery.

We're very excited!

Sue and Mark

Cross Border Medical Tourism

Cross Border Medical Tourism services is for those people who want to be considered for Zhittya's future clinical trials or its current Medical Research Studies. Cross Border's focus is to fill all available slots in the Medical Research Studies in the British Virgin Islands and The Bahamas, while we wait for other clinics to come online.

Cross Border is working on filling the available slots for the next BVI Medical Research Studies (intranasal FGF-1 for Parkinson's disease) on the following dates:

Cohort #31: December 9 – 14, 2024

Cohort #32: January 7 – 12, 2025

Cohort #33: February 4 – 9, 2025

Cohort #34: March 10 – 15, 2025

I am showing cohorts further out in time since we are filling up faster and have fewer spots open each month.

Please contact Sam Cross at Cross Border Medical if you wish to be considered for the BVI cohorts or slots in The Bahamas. Sam's email address is:

sam.crossbordermedical@gmail.com.

In addition, if you are interested in participating in the brain scan studies which will take place at Washington University in St. Louis, please let Sam know. There are a finite number of slots for the imaging studies. These studies will look at brain blood flow before and after treatment with FGF-1. There has been no reported pain associated with the MRI scan.

Heart Disease Clinical Trials and Medical Research Studies:

Zhittya is proud to announce that it is beginning its active recruiting and selection process for patients suffering from late-stage heart disease. FGF-1 was originally used in USA FDA clinical trials to treat severe coronary artery disease. The treatment was shown to be safe and a potentially efficacious treatment for those suffering from coronary heart disease. Watch this ABC Nightly News' clip on Zhittya's drug being used for the heart indication:

https://www.youtube.com/watch?v=IPtv_OLWK4k

Zhittya is now actively recruiting patients to participate in Zhittya's Medical Research Studies in The Bahamas, as well as future USA FDA clinical trials. If you are interested in participating in these studies, please reach out to Sergiy Montano, our Vice President of Marketing at: sergiy@zhittyamedicine.com and he will assist you from there.

Pre-IPO Private Placement

Bart Vossen is still working with people interested in learning more about the Pre-

IPO placement we are conducting. If you are an investor and wish to learn more, please email Bart at: bhvossen.rmena@gmail.com

We will be closing the Pre-IPO Placement at the end of December 2024.

Upcoming events:

Presently, we have nothing pending but will keep you posted in future Monthly Updates.

Dr. Jack Jacobs

Traumatic brain injury (TBI) is a unique neurodegenerative condition that is associated with repetitive mild traumatic brain injury. Repetitive closed head injury occurs in a wide variety of contact sports, including football, boxing, wrestling, rugby, hockey, lacrosse, soccer, and skiing. In collision sports such as football and boxing, players may experience thousands of sub-concussive hits over the course of a single season. Furthermore, additional large groups of individuals prone to repetitive head trauma, such as combat military veterans, may be at risk for TBI.

Most sport-related head injury is minor and although the majority of athletes who suffer a concussion recover within a few days or weeks, a number of these individuals will go on to develop long-lasting or progressive symptoms. This is especially true in cases of repetitive concussion or repetitive mild traumatic brain injury in which at least 17% of individuals develop encephalopathy (TBI), and this number may be an underestimation of the problem. It is unclear what severity or recurrence of head injury is required to initiate TBI; no well-designed prospective studies have addressed these important issues. The severity of the disorder

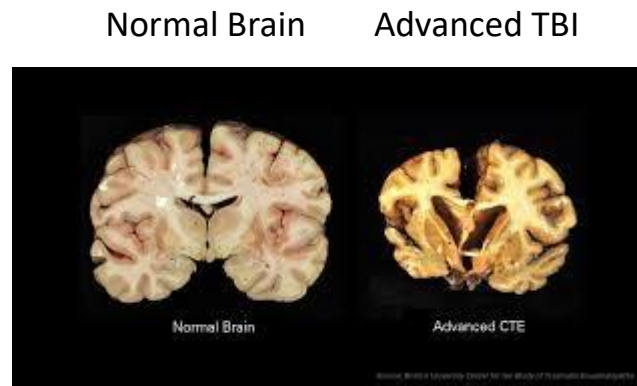
appears to correlate with the length of time engaged in the sport and the number of traumatic injuries, although whether a single traumatic brain injury can trigger the onset of TBI remains a matter of speculation.

TBI was originally reported in 1928 by a New Jersey pathologist (Martland, 1928) who described the clinical aspects of a progressive neurological deterioration (“punch drunk”) that occurred after repetitive brain trauma in boxers. TBI is associated with symptoms of irritability, impulsivity, aggression, depression, short-term memory loss and heightened suicidality that usually begin 8–10 years after experiencing repetitive mild traumatic brain injury. With advancing disease, more severe neurological changes develop that include dementia, gait and speech abnormalities and symptoms resembling Parkinson’s disease. In late stages, TBI may be clinically mistaken for Alzheimer’s disease or vascular dementia.

The evidence suggests that TBI begins at a defined focal area in the brain, usually adjacent to small blood vessels and in the cerebral cortex, an area of the brain that plays a key role in memory, attention, cognition and language. The disease spreads slowly over decades to involve widespread and diverse regions of the brain, including areas of the brain that control long-term memory, executive functioning and dopamine production. The neuropathological changes of TBI are distinctive and easily distinguished from other neurodegenerative diseases, including Alzheimer’s disease. There is a distinctive pattern of neurofibrillary tangles (composed of phosphorylated-tau proteins) seen in TBI, which differs from Alzheimer’s disease. In addition, β -Amyloid ($A\beta$) deposition, which is a hallmark of Alzheimer’s disease, is not consistently seen in TBI. Over time,

neuronal loss becomes substantial in TBI and can result in a significant decrease in brain volume as is apparent in Figure 1 below.

Figure 1: *Autopsy specimens of a normal brain and a brain with advanced TBI*



Presently, there are no available biomarkers for the diagnosis of TBI. However, advances in neuroimaging, most notably the development of PET scanning procedures that can image tau-containing neurofibrillary tangles, offer the promise of detecting TBI in its earlier stages. As shown in Figure 2 below, PET scanning with an investigational fluorescent tracer (termed FDDNP) which binds specifically to the tau protein in neurofibrillary tangles may reveal chronic traumatic encephalopathy (CTE) in individuals and differentiate it from Alzheimer's disease.

Figure 2: *Pet scan showing neurofibrillary tangles (non-blue color) in normal individuals and patients with TBI (suspected CTE) and Alzheimer's disease.*



Microvascular Dysfunction in Chronic Traumatic Encephalopathy

Recent research has indicated that for two neurodegenerative diseases, Alzheimer's disease and Parkinson's disease, a critical early and possible precipitating event is dysfunction in the microvasculature leading to hypo-perfusion and a diminished capacity of brain neurons. In probably the largest study of its kind, researchers from McGill University in Montreal recently completed a study in which they followed disease progression in 1171 patients with Alzheimer's disease. They developed a 30-year trajectory for biomarkers of Alzheimer's disease and reported that the very first changes seen in the disease was a deterioration of the microvasculature leading to under-perfusion of brain neurons. These vasculature changes occurred before any of the symptomatic changes in Alzheimer disease occurred, including structural changes in the brain, accumulation of beta amyloid plaques or cognitive decline.

With Parkinson's disease, research being conducted at the University of Southern California has recently led to the hypothesis that microvascular dysfunction in the brain and flaws in the blood/brain barrier may lead to the damage and ultimate

destruction of selected population of neurons, including the dopamine-producing cells that are depleted in Parkinson's disease.

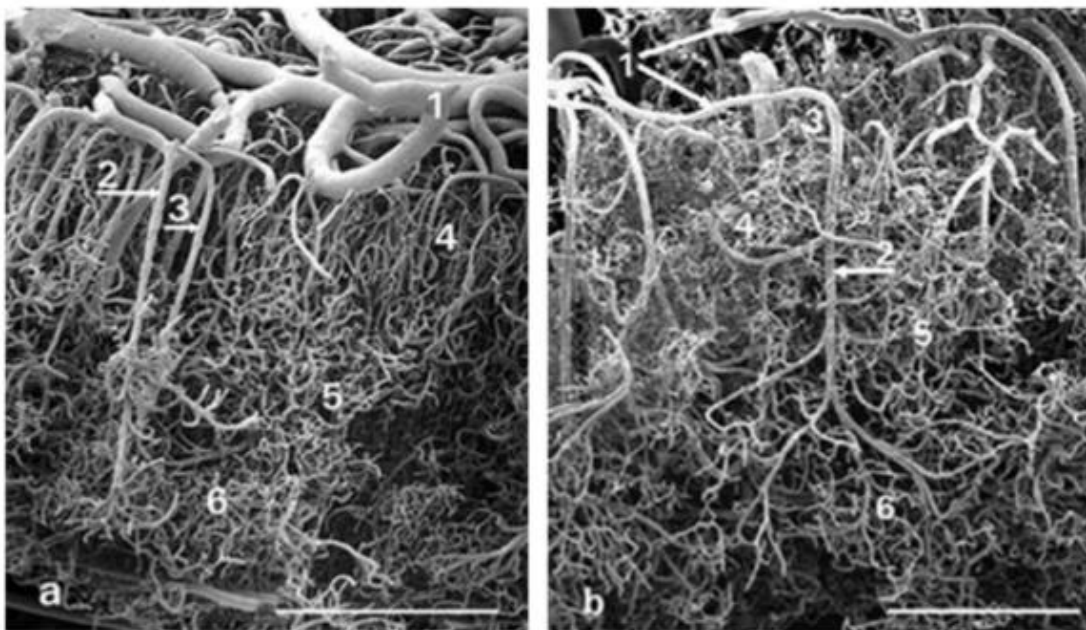
What is the evidence that disrupted blood perfusion in the brain has any link to the initiation and progression of TBI? There are several lines of evidence that point to a strong link between vascular dysfunction and TBI. In human brain specimens taken at autopsy from TBI victims, microvascular disruption is seen almost universally. Prominent cerebral microvasculature pathology was reported in some of the first cases of TBI described by Corsellis in 1973. Extensive microvascular dysfunction was also reported in active-duty military service members with TBI who had been exposed to multiple blast explosions. Finally, striking vascular changes have been seen in specimens from sports-related cases of TBI.

To date, no studies have examined in living subjects the extent of microvascular damage in the early stages of TBI. However, there is very strong evidence of a link between under-perfusion of brain neurons and subsequent impairments from medical research into the pathophysiology of traumatic brain injury (TBI). Both in animal models of TBI and in patients with TBI, direct and long-lasting damage to the microvasculature of the brain can be demonstrated.

As seen in Figure 3 below, scanning electron microscopy from a patient with TBI indicates a remarkable disordering of the cerebral vasculature. The left panel shows the microvasculature from a normal area of the brain while the right panel shows a micrograph from a damaged area of the brain. From Figure 3, it is readily apparent that with TBI there is a collapsing and flattening of small arteries in the microvasculature (areas labelled #1 in both panels) as well as a gross disordering

of the smaller capillaries which would nourish adjacent neurons (areas labelled #4 in both panels).

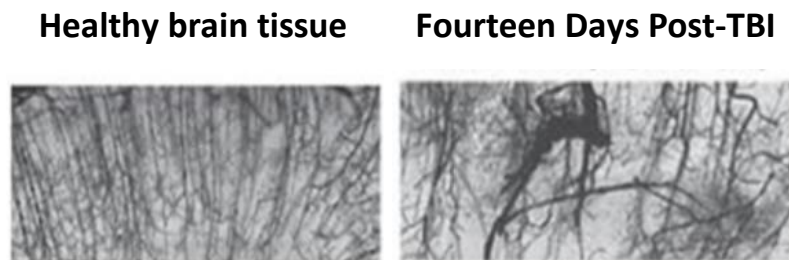
Figure 3. *Scanning electron micrograph of brain tissue from a patient with TBI. The left panel is a section from healthy uninjured brain and the right panel is from an area of the brain with TBI. In the TBI panel, note the severely shrunken and flattened arterioles (area labelled #1) and the general disordering of the capillary bed).*



Striking microvascular disordering has also been consistently observed in animal models of TBI. As shown in Figure 4 below, rodents that have been subjected to experimental TBI and then allowed to recover showed a microvasculature that is less dense and more disordered. In these experiments rodents were subjected to pressure-induced fluid percussion TBI, allowed to recover and then the brain microvasculature was examined 24 hours and 14 days post-injury.

Figure 4. *Histological analysis of small blood vessels in brain tissue from rodents subjected to experimental traumatic brain injury. The left panel displays capillaries visualized in the normal brain, and the panel on the right side shows the microvasculature fourteen days after the animals received a traumatic brain injury.*

Microvasculature in the Brain



From the above results, it could be anticipated that neurons would most likely be under-perfused in those areas of recovery which display a disordered microvasculature. In addition, it is also not hard to imagine that if this trauma was repeated continuously the accumulated microvasculature damage would lead to diminished neuronal functioning and ultimately, nerve cell death, a condition that is consistent with chronic traumatic encephalopathy.

Angiogenesis – A Treatment Modality for TBI That Should Be Examined

Angiogenesis is a natural regenerative process that the body uses to produce new blood vessels in damaged tissues or organs. Angiogenesis is controlled by a number of growth factors and cytokines, and these factors (and their cell surface receptors) are upregulated in response to injury or ischemia. Probably one of the most potent known stimulators of angiogenesis is the human protein, FGF-1. This growth factor is part of a large family (22 members) of proteins termed fibroblast growth factors. FGF-1 is the only member of this family that can activate all 7 cell

surface receptors that mediate the biological activities of the FGF family, making it a growth factor that has highly diverse activities in the body. FGF-1 also is a potent inducer of the production of other cytokines that are involved in tissue repair and regeneration, setting off a cascade of metabolic activities critical for tissue repair and healing.

Therapeutic angiogenesis is the use of angiogenic agents such as FGF-1 to stimulate new blood vessel formation in tissues and organs damaged by a lack of blood perfusions. FGF-1 has enjoyed remarkable clinical success in a number of USA FDA-authorized clinical trials, including severe coronary artery disease and diabetic foot ulcers, with both disorders a result of poor blood flow. FGF-1 was in Phase II clinical trials before its clinical development was suspended due to financial reasons (and not for clinical efficacy or safety reasons). As Dan showed in his first figure above, a characteristic “blush” of newly formed blood vessels is seen when FGF-1 is injected into the hearts of patients with coronary artery disease. It was also established that the newly grown blood vessels were still functioning 3 years after treatment and that patients enjoyed a significant improvement in clinical markers, including exercise performance, angina scores and quality of life indexes. Given our contention that damage to the microvasculature in the brain is a contributing factor in the development of TBI, clinical studies with FGF-1 in TBI patients make sense.

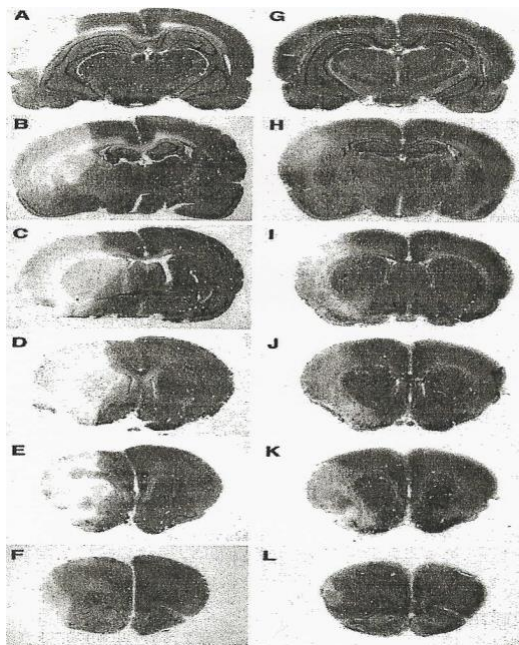
FGF-1 is Neuroprotective and Neurotrophic

As mentioned above, FGF-1 has diverse biological activities and in addition to its angiogenesis properties there is a large body of medical literature that has established that FGF-1 can not only protect neurons from harmful stimuli (such as

hypoxia during stroke) but can also stimulate the production of neural stem cells and new neurons in the adult brain. Figure 5 below shows the neuroprotection that FGF-1 can provide in an animal model of stroke, where IV administered FGF-1 resulted in mice that had a much smaller stroke area. These studies also demonstrate that FGF-1 can cross the blood brain barrier to gain access to areas of the brain affected by stroke.

Figure 5: *Effect of FGF-1 treatment in a focal animal model of acute stroke.*

Placebo-treated FGF-1 treated



As shown in the figure above, sectioning through the brain followed by subsequent staining of the brain tissue allowed a visualization of the stroke infarct. The infarct area appears as a white area in the slices and the effect of FGF-1 in reducing infarct volume is readily apparent.

In addition to its neuroprotective properties, FGF-1 has been shown in animal studies to stimulate neurogenesis, a process characterized by the development of

new neuronal stem cells and their maturation into functioning nerve cells. Mice who had been given a permanent stroke lesion, followed by 4 weeks of FGF administration, developed an increase in brain axonal sprouting and subsequent enhanced recovery of motor function, including limb movement and coordination in mice. As TBI is characterized by damaged neurons and neurons at risk of dying, this additional neuroprotective activity of FGF-1 enhances its attractiveness to test as a possible therapy for this disease.

Conclusion by Dan Montano

Zhittya has made great progress these last 12 months. Almost 200 Parkinson's disease test subjects, two patients with dementia, one patient with Alzheimer's disease, two patients with autism, and one patient with ALS are advancing along our pathway of discovery.

In 2025, we should be completing our animal testing for the utilization of FGF-1 for:

- 1) Heart disease (for USA FDA Phase II)
- 2) Brain disorders (USA FDA Phase I)
- 3) Type-2 diabetes
- 4) Clinical leg ischemia
- 5) Lung disorders

All of these indications need animal testing to comply with the FDA requirements to conduct human clinical trials to seek FDA approvals for our medicines. FGF-1 has been utilized in four human studies (two in Germany and two in the USA) with zero adverse events and amazing improvements in heart function for the no-option heart patients that were treated, and yet we have to go back and redo

animal studies again for the FDA.

I believe 2025 will be a wonderful year for Zhittya's progress and our creation of the proof to accelerate getting our medicines approved so we can get them to patients with all of these diseases.

One personal comment: Above in the patient section, Bobby discussed his improvements. We talked on the phone a few weeks ago, and he told me that his golf game has improved since starting the treatment. He said in a recent golf tournament he finished 3rd. He was hoping, with ongoing FGF-1 treatments, he could finish first. I do not know if our FGF-1 treatment will improve his golf game, but what I do know is two years ago his hand shook so violently he could not shave himself. Today, he can shave himself and apparently putt better than me. The only time I ever came in 3rd playing golf was when only two of us were playing.

I want to thank Bobby and all of our Parkinson's disease test subjects as each one of them is a "Warrior!" The path of discovery relating to the question of whether we can treat Parkinson's disease is complex and full of additional problems; people with Parkinson's disease also have hip replacements, back surgery, hospitalization from COVID-19 and more. As test subjects start to feel better from the FGF-1, and they start a difficult effort of trying to reduce their medicines, they often struggle with fear and doubts. When a test subject tells me their tremors are still present after nine months of FGF-1 dosing, it breaks my heart. When they then tell me they have reduced their Parkinson's medicines by 80%, I cry for joy; as I know that is good for them and their long-term health. This journey of discovery is like walking through a dark cave, without a light to see where we are

going. With every step, we have to be careful. When one of our test subjects gives us a report, it is like a light showing us a safe path for a few more steps. I look forward to all the people we treat with FGF-1 who are suffering with Parkinson's disease now, playing golf with Bobby in the future. Then I will know we have all won!

Bless you all!

Dan Montano, CEO

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