T.E.N.T. – Targeted Electrovalent Nano Therapy - A Novel Approach to Cell Mediated and Humoral Immunotherapy utilizing Nano Metallic Silver Tetrahedral Tetraoxide.*

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ABSTRACT: Targeted Electrovalent Nano-Therapy ("T.E.N.T.") involves the use of highly uniqe Nano-Metallic Silver particles which are capable of targeting pathogens at the molecular level with a highly sophisticated and reactive electrostatically charged surface coating of Silver Tetrahedral Tetraoxide. These Nano Silver particles have been clinically shown as safe for human ingestion and injection as well as additive and synergistic to probiotic bacteria. They are also deadly to a very broad range of pathogens including numerous Coronaviruses. Even more importantly, no bacterial resistance has ever been demonstrated with this highly proprietary Silver Nano technology. Based on a long history of efficacy and performance and its powerful antimicrobial preservative nature, we believe that this Nanotechnology could be utilized as a vaccine adjuvant to replace many of the much more cytotoxic substances such as 2-phenoxyethanol, benzethonium

**** Submitted to ABL Board of Directors March 15, 2017 and re-edited in April 2020.***

chloride, aluminum phosphate, potassium aluminum sulfate, monophosphoryl lipid A, formaldehyde and or thimerosal. We believe the T.E.N.T. Nanoparticle has the ability to target and kill pathogenic bacteria and viruses created by antigenic drift and or antigenic shift while allowing the vaccine to more efficiently stimulate the production of B and T cells against its specific viral and bacterial epitopes.

Central to the concept of T.E.N.T. is the use of a proprietary Nano-Silver technology referred to as Nanometallic Silver Tetrahedral Tetraoxide ("N.M.S.T.T.O "). This N.M.S.T.T.O particle has a solid metallic core which ranges b/w only 5-7 Nanometers (Nm) in diameter (5-7 Billionths of a meter) and has a patented resonance frequency (b/w 890-910 TeraHertz - the same as Ultraviolet Light A+B frequency). This N.M.S.T.T.O particle has a powerful electrostatic, nano-catalytic mode of action with a broad range of bacteriocidal, virucidal and fungicidal capabilities without causing harm to the host or probiotic bacteria. Leveraging these capabilities, VeraSIL Therapeutic Research, Inc.,** has developed a proprietary new "Targeted Electrovalent Nano Therapy" or "T.E.N.T." for the vaccine market to try and help eradicate vaccine preventable infectious diseases and fight global pandemics. We believe that when T.E.N.T., is combined with either humoral or cell mediated vaccines (as an adjuvant or preservative) the highly unique cellular mechanisms of action of the N.M.S.T.T.O particle and its profound level of efficacy against a broad spectrum of microorganisms (without toxicity to the host) make it capable of killing all antigenic

***** VeraSIL Therapeutic Research, Inc. is ABL's exclusive Licensee for NMSTTO in the Dental, Dermal Filler, Botulinum Neurotoxin, Vaccine and Surgical/Exam Glove Markets.***

variants of a particular pathogenic infection. In other words, when the T.E.N.T. Nanoparticle is combined with a Vaccine, it creates the potential for a "Universal Vaccine" capable of not only more efficiently stimulating the production of B and T cells against specific attenuated or inactivated antigens but, capable of killing all the circulating antigenic variants as well.

American BioTech Labs ("ABL") is the sole manufacturer of this Nano Silver particle which is FDA and Health Canada cleared in various formats and has a unique silver tetrahedral tetraoxide surface coating which has a powerful, electro-static, nano-catalytic mode of action, proven to kill a broad range of microorganisms without causing harm to the host. The highly charged crystalline lattice oxide coating generates its own magnetic field evident in Transitional Electron Microscopy (TEM).

The combination of this highly "charged" silver tetraoxide surface layer and the specific Resonance Frequency of the N.M.S.T.T.O particle creates this strong magnetic field which interferes with the multivalent charges of various amino acids and or polypeptide structures (and their associated hydrogen bonds) located on the cell wall of various pathogenic microorganisms. This electrostatic interference disables these pathogens and prevents them from effectively communicating with one another and or from entering or "keying" with the host cell and replicating. Others have demonstrated that the highly charged crystalline lattice oxide layer of the N.M.S.T.T.O particle disturbs the cell wall/ membrane permeability of these pathogenic organisms, so once inside the cell, this N.M.S.T.T.O

particle creates significant oxidative stress and effects the respiration functions within the cytoplasm and the nucleoid as well as interference with replication of the chromosome and its associated proteins and RNA. No replication means the end to the propagation and transmission of the disease.

There are well over 400 published studies of bacterial and viral challenge tests conducted by over 60 independent companies, labs, universities, and government institutions that demonstrate quick acting 4 and 5 log reductions of the N.M.S.T.T.O against a wide range of micro- organisms including; Malaria, various Influenza A strains including H1N1, H3N2 & H5N1. Successful in- vitro lab testing has been completed against the HIV lentivirus, Staphylococcus aureus, Pseudomonas aeruginosa, Escherichia coli, Hepatitis B (effective against both Reverse transcriptase and DNA Polymerase methods of replication) and many drug resistant bacteria including C.R.E, M.R.S.A., V.R.E., and all 8 strains of the MDR pleomorphic aerobic gram- negative bacillus Acinetobacter Baumannii. N.M.S.T.T.O therefore makes for an excellent preservative / stabilizing agent especially when human ingestion and injection studies show that the N.M.S.T.T.O is not harmful to biological tissues. The N.M.S.T.T.O particle has numerous FDA 510(k) clearances for use as a broad spectrum anti-bacterial agent as both an OTC and Prescription strength “surgical wound wash and irrigant” and “wound healing hydrogel” as well as a disinfectant for use in medical device insertion sites, surgical incisive wounds, donor and recipient graft sites. N.M.S.T.T.O is not a

drug and is **not metabolized by the body** - it is excreted via the liver and kidneys due to particle size.

Over the past 14+ years a Reconstructive Dental Surgeon named Dr. Andrew Willoughby from Langley, B.C., Canada has successfully performed in excess of 55,000 invasive peri-osseous surgeries (in contact with vascular, adipose, osseous, connective, and nervous tissues) using N.M.S.T.T.O as a wound healing, disinfectant agent. It was the overwhelming lack of material adverse effects combined with the aforementioned in vivo and in-vitro data, that lead to a phase 1 human clinical trial where a pH adjusted solution of 10ppm N.M.S.T.T.O was used as a diluent to reconstitute a Botulinum Neurotoxin protein called OnaBotulinum Toxina A marketed and sold under the tradename of Botox$^{R***.}$ These Phase 1 human trials demonstrated that the N.M.S.T.T.O solution could be successfully combined with a purified protein. The result was a stable complex capable of extending both efficacy and performance of the Botulinum Neurotoxin. In excess of 15 International Patents have now been issued on the novel reconstitution of Botulinum Neurotoxin with NMSTTO (instead of .9% Neutral buffered Saline). The most recent is Patent 10,864,321 issued by the US Patent and Trademark Office on December 15, 2020. This Nano Silver solution also meets USFDA USP 51 Guidelines for an Antimicrobial Preservative under 21 CFR Part 58 so, it makes for an ideal injectable preservative for numerous Botulinum Neurotoxins and other injectable solutions.

*** BotoxR is a registered trademark of Allergan Plc and Abbvie, Dublin Ireland.

It was Dr. Willoughby's extensive use of this Nano Silver technology with Botox^{R} that lead to his realization that this Silver Nanoparticle may have a similar effect on another class of injectable proteins – namely vaccines.

In general, Vaccines are able to combat a variety of pathogenic bacterial and viral diseases by using either inactivated, attenuated, DNA plasmid or recombinant portions of specific pathogens or proteins to stimulate an antibody-mediated response involving B-Cells so that subsequent encounters with this same pathogen/antigen generates a system wide B memory cell response. This is the essence of targeted humoral vaccine immunotherapy. The problem with many of these infections is that they develop either antigenic drifts (accumulated mutations affecting the efficacy of antibody binding sites most commonly found in Influenza A, B and C sub types) or the more distinct antigenic shifts (involving replacement of viral attachment protein enzymes found in different Influenza A sub types). Both create antigenic variations which the body's immune system does not completely recognize and therefore abrogate the binding of select antibody Fragmented Antigen-Binding ("FAB") regions. In much the same way as bacteria develop drug resistant Antibiotic strains, many Vaccines (not just Influenza but Rhinovirus, HIV and some cancer causing viruses) are just as vulnerable to Antigenic drifts and Antigenic shifts. Once a pathogen/antigen invades the host cell however, the body utilizes a different type of immune response to fight this infection – one that is T-cell mediated rather than antibody mediated. Many Influenza A sub-types / strains can be effectively targeted by antigen specific ligation of T-cells receptors at specific N2H2D nucleoproteins and

PAH2D acid polymerase sites. Although T-cell mediated immunity can promote viral clearance through apotosis and the release of anti-viral cytokines, it does not provide sterile resistance because unlike humoral immunity, it cannot prevent the pathogen from entering host cells(1).

As an alternative to this ongoing problem with Targeted Immunotherapy we have developed a new approach called “Targeted Electrovalent Nano Therapy” (“T.E.N.T”). T.E.N.T. utilizes the broad reaching anti-viral, anti-bacterial and anti-fungal properties of a proprietary ultra dilute N.M.S.T.T.O particle which can be used to target and kill specific viral or bacterial pathogens as well as any antigenic variant strains of that particular disease which might re-infect the host. Our in vivo test data from seven AIDS patients appears to indicate that the N.M.S.T.T.O particle is both an effective anti-viral and virucidal agent. NMSTTO not only has demonstrated an ability to kill the HTLV3 virus but, it is also capable of neutralizing the HIV lentivirus by inhibiting its development and replication. The AIDS report which was published by Dr. B.M. Hedge et al also demonstrated that the NMSTTO has the ability to modulate the immune system by producing more T-cells. To be both virucidal and anti-viral is highly unique.

Additionally, due to the heightened efficacy and performance of the N.M.S.T.T.O particle against a very broad range of yeast, mold, fungi, bacteria and viruses, T.E.N.T., has the potential to act as a superior preservative and adjuvant for the vaccine because it is also non-toxic to human tissue. Further evidence of its non toxicity is demonstrated in a recent Human ingestion (time exposure) study (now published in

PubMed) on 60 healthy patients who were orally dosed with 10 ppm N.M.S.T.T.O.(2) All 60 patients showed no changes in metabolic, blood counts, sputum induction, urinalysis, or on either chest and abdomen digital MRI's. Silver serum and urine content were also determined in this same study showing no morphological changes detected in the lungs, heart or abdominal organs. No significant changes were noted in Pulmonary reactive oxygen species, or in pro-inflammatory cytokine generation - All indications of non-toxicity.

The primary mode of action for the NMSTTO particle is "Nano-catalytic" rather than chemotherapeutic so, there is no known resistance to this unique Nano particle. N.M.S.T.T.O is also proven to eradicate Fungi such as Aspergillus niger and Candida albicans with a 5 log reduction in less than 1 hour. We have in-vivo Oral DNA biometric test data which demonstrates a dramatic reduction in the levels of some of the most aggressive gram positive / gram negative anaerobic periodontal pathogens including; Treponema denticola, Tannerella forsythia, Porphyromonas gingivalis and Peptostreptococcus micros- all without harming probiotic bacteria. In addition, independent clinical tests show the N.M.S.T.T.O particle to be effective against HSV1 (Herpes Simplex Type 1), as well as S.A.R.S., Tuberculosis, Varicella Zoster, Dengue virus and the M.E.R.S. Coronavirus.

We now know that the N.M.S.T.T.O's ability to breakdown / destroy bacteria and viruses and their associated biofilms is related to the proprietary manner in which the N.M.S.T.T.O particle is manufactured.

During ABL's N.M.S.T.T.O manufacturing process the ultrapure water source is treated with Reverse Osmosis (RO) down to a level of .24 ppm Total Dissolved Solids (TDS). This creates highly 'reactive' water which is lacking electrons. When Hi energy Silver Nanoparticles are added back into this ultrapure water source an inter-molecular dispersion of energy is created between the Ag404 molecule and the water molecules by sharing the oxygen molecule via covalent and trivalent bonds. These Van Der Waal electromagnetic forces create semi-permanent bonds between the Ag404 and H20 molecules which are hard to break. The formation of long chain structured water molecules (3) allows for the dispersion of the N.M.S.T.T.O's resonance frequency and highly reactive electrovalent charge throughout the volume of water via what we have termed as a "High Energy Nanosonic Dynamic Dispersion Field". ("H.E.N.D.D.F."). The elimination of Biofilm using N.M.S.T.T.O has been independently confirmed by a peer reviewed research paper entitled "The Ability of a Colloidal Silver Gel Wound Dressing to Kill Bacteria In Vitro and In Vivo" where the authors concluded that the Ag-gel (N.M.S.T.T.O) was effective in preventing biofilm infections caused by both Gram negative and Gram positive bacteria as well as there associated Biofilms(4). Because of the rapid and complete elimination of many aggressive anaerobic pathogens and the rapid reattachment of connective tissue we have clinically observed, we believe that the H.E.N.D.D.F., of the N.M.S.T.T.O particle is acting to mechanically disrupt bacterial and viral biofilms on an ultra-compact, Nano-sonic frequency of 890-910 TeraHertz. It is this unique electrovalent feature which accounts for the ability of the ultra dilute N.M.S.T.T.O particle

in water to generate such rapid and complete kill rates and log reductions.

The combination of this highly “charged” silver tetraoxide surface layer and the specific Resonance Frequency of the N.M.S.T.T.O particle creates a strong magnetic field which interferes with the multivalent charges of various amino acids, polypeptide and polysaccharide structures (and their associated hydrogen bonds) located on the cell wall/ membrane of various pathogenic microorganisms. This electrostatic interference disables these pathogens and prevents them from effectively communicating with one another and from entering or “keying” with the host cell and replicating. Others have demonstrated that the highly charged crystalline lattice oxide layer of the N.M.S.T.T.O particle disturbs the cell wall / membrane permeability of these pathogenic organisms, so once inside the cell, this N.M.S.T.T.O particle creates significant oxidative stress and effects the respiratory functions within the cytoplasm and the nucleoid replication of the chromosome and its associated proteins and RNA. No replication means the end to the propagation and transmission of the disease.

We believe that the most obvious and immediate use of T.E.N.T., would be to combine it with a Vaccine to help stabilize and preserve the Vaccine against bacterial degradation the same way we have demonstrated this by reconstituting N.M.S.T.T.O with Botulinum Neurotoxin. We have Scanning Electron Micrographs (SEMs) showing that the Silver Nanoparticle can in fact envelope and encapsulate Type 2 Collagen providing it with a protective layer and preventing it from

becoming susceptible to atmospheric, microbial and thermal degradation. We believe that this, is in part, why we have seen reconstituted Botox solutions remain viable for upwards of 3-4months (instead of weeks) after being reconstituted. We believe that the Silver Nanoparticle may also offer protection from endocnucleases and against thermal breakdown which is of known concern with many of the more labile recombinant vector vaccines.

Such a compound could also help prevent cross contamination of the Vaccine from multiple withdrawls from the same vial. Based on our clinical findings and research data to date, we believe that the use of the N.M.S.T.T.O compound is also safer and more efficacious than current Vaccine preservatives including; phenol, 2-phenoxyethanol, benzethonium chloride, aluminum phosphate, potassium aluminum sulfate, monophosphoryl lipid A, formaldehyde and or the ethyl mercury derivative called thimerosal. Although thimerosal is still used as an adjuvant in many Influenza vaccines, Antibiotics such as Gentamycin, Streptomycin, Neomycin and Amphoteracin B are now viewed as preferred Adjuvants. The problem with many of these Gen 2 and Gen 3 Antibiotics is developing bacterial resistance which is why Beta Lactamase inhibitors are now being added. The problem continues to be that the broad based and indiscriminate use of vaccines which utilize Antibiotics adjuvants (for which there is known bacterial resistance) is more of a hindrance than a help. As previously mentioned, this Silver Nanoparticle meets the FDA USP 51 Guidelines for an Antimicrobial Preservative under 21 CFR Part 58 and there are no known bacteria, yeast or viruses that it cannot kill.

The more ‘involved’ concept would be to utilize T.E.N.T., as a Vaccine adjuvant so it not only provides inherent preservative capabilities but can also be used to treat patients with active disease and or antigenic variants. We believe that IF the adjuvant already has the ability to kill the antigenic variants of the disease then the Vaccine and the body’s immunological response should be able to more effectively stimulate antibody production. In fact, our clinical research with Botulinum Neurotoxins shows that the highly reactive super oxide layer of the N.M.S.T.T.O particle may also have an ability to block TLR5 and MyD88 receptors and down stream pro-inflammatory cascades which independent vaccine researchers believe help generate greater T-cell activation and B-cell abundancy - both important features in the body’s adaptive immune responses(5).

While the vaccine would be present to boost/stimulate the hosts natural humoral response to infection, an adjuvant of N.M.S.T.T.O particles could effectively lower any residual antigenic bacterial/viral load or partially recognized antigens due to ‘mutational drift’ and or ‘shift’– the addition of this new N.M.S.T.T.O compound in essence, might help create an active ‘virucidal’ or ‘bacteriocidal’ vaccine with ‘built in’ preservative capabilities. This is a similar concept to the cross protective cell mediated immunity found in some H5N1 Bird populations (6). Because of the H.E.N.D.D.F. concept and the ultra dilute number of N.M.S.T.T.O particles required to effectively kill a pathogen, we believe that a single normal vaccine dosage should contain more than an adequate amount of N.M.S.T.T.O to be efficacious for both humoral and cell mediated vaccines.

Antigenic drift due to “immunologic pressure” (which drives evolution of the virus from cross protective strains) is also a concern with a CD8 + T-cell vaccine approach. In this scenario, the mutation of an NP epitope that binds HLA B35 present in older viral Flu strains indicates that immunologic pressure from cross protective CD8+T-cells can drive the evolution of the Influenza virus. (7) We believe that using T.E.N.T., as an adjuvant could also help a CD8 + T-cell mediated Vaccine, develop a sterile resistance capability by effectively targeting and neutralizing the antigenic epitopes before they enter the cell. This may help promote cell-mediated immunity which may be more favourable in fighting potentially lethal highly pathogenic influenza strains. (8) The notion of a “universal” cross protective cell mediated immunity for highly pathogenic strains is potentially a break through therapy.

In the same way as antiviral drugs and antibiotics are used to treat disease once it has manifested clinically, the N.M.S.T.T.O particle has this same broad spectrum anti-bacterial, anti-viral, anti-fungal ability but, it is also ‘immune’ to bacterial resistance (ie. 4-5 log reductions with some of the most aggressive superbugs in existence including VRE, MRSA and CRE – all within 30 minutes.) When it comes to Influenza A+B viruses for example, N.M.S.T.T.O particles are not selective based on antigenic variations in glycoproteins such as hemaglutinin or neuraminidase, the same way most Vaccines are – instead, they are ubiquitous.

Extensive IP has been filed on the aforementioned subject matter.

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