"The Journey of Bravado Pharmaceuticals and the
Development of CoVer Nasal Antibody Drops"

Transforming an empty warehouse into a fully licensed pharmaceutical company is a challenge anytime, and especially in the months leading up to a global pandemic. I purchased the building that would ultimately become Bravado Pharmaceuticals on 11 Oct 2018, with big dreams of creating a state-of-the-art facility for the development, manufacturing, and testing of pharmaceuticals. As Albert Einstein was famously quoted, "imagination was more important than knowledge". When I "closed" on the building in the following days, I had a lot of imagination working but little knowledge of the coming obstacles. Imagination and creativity have been integral parts of each step in "Creating Bravado Pharmaceuticals" and the pathway that led Bravado to develop CoVer Nasal Antibody Drops.

Initially, I was told the buildout of the labs, process rooms and manufacturing areas might take six months. After seventeen months of construction and permitting delays, we finally celebrated our official grand opening on 02 Mar 2020. However, the world had other ideas because, within a week, the Covid-19 (CV-19) global pandemic began. With an uncertain future, I sent my employees "home" and began advertising on LinkedIn that my new, fully equipped pharmaceutical company was willing to do pro bono work for covid-related projects. On 11 May 2020, I received an email from a former colleague. We had worked together to develop a potential oral vaccine years earlier, and he knew I had developed the anti-viral Rapivab for Biocryst Pharmaceuticals, Inc. in 2009 to combat pandemic H1N1. Rapivab was developed in solution, suspension, and lyophilized form with the lyophilized form ultimately stockpiled by the US government for emergency use against the avian or seasonal flu.

My colleague thought Bravado might be a good candidate to help with the CV-19 pandemic. When he reached out to me and explained the concept of "CoVer Nasal Antibody Drops." "CoVer" was an idealogical concept created as an inexpensive solution and alternative to the "race to a vaccine". Stanford University Palo Alto and SPARKGLOBAL (a translational medicine non-profit group which encompasses groups from 8 continents and now includes Bravado) were seeking help with the concept of "CoVer". The program was led by Professor Daria Mochly Rosen of Stanford and Head of SPARKGLOBAL with Charles River Laboratories supplying the antibodies to whoever was chosen to formulate the product into a nasal drop system. Bravado was fortunate to be chosen.

In the initial stages of infection of CV-19, SARS-CoV-2 targets nasal and bronchial mucosal cells through the viral spike protein that binds to the angiotensin converting enzyme 2 (ACE2) receptor on the host cells in the nasal cavity. Through this binding action, the virus enters the host cell. The proposed action of the product to be formulated and developed by Bravado would be to perform an antibody nasal blockade where the "antigen" antibody blocks the ACE receptor sites.

Using my past experience developing nasal products in the 1990's for Bausch and Lomb, I was able to quickly determine a starting point for the product. Initial formulation studies at Bravado centered on development of a proper suspension vehicle with suitable retention in the nasal cavity. Various grades of microcrystalline cellulose (MCC) and sodium carboxymethyl cellulose (Na-CMC) to were investigated to achieve proper viscosity for nasal retention up to 8 hours. After evaluation of four products, it was determined Vivapur MCG 591P (a co-processed composite of MCC and Na-CMC) yielded the proper rheological profile. Formation of the suspension required dual agitation by over-head mixing combined with homogenization.

The next part of formulation development targeted making the pharmaceutical vehicle isotonic to reduce irritation to the nasal mucosa and avoid induction of osmotic flow. Sodium chloride 0.9% is commonly used to create physiological osmolality of 290 mOsm and was used in the formulation. At the 0.9% level, after combination of the suspension phase with the "antibody phase" of the formula, the product was isotonic.

During formulation, Bravado developed an HPLC method to quantify the IGY protein recovery in the proposed formulas. We determined the best way to calculate recovery for the material was to calculate based on the area of the largest peak as it theoretically yielded the most accurate and precise result of all the peaks. The final product was also sent out for bioburden and microbial testing.

The final product consists of Vivapur MCG 591, IgY Protein, Sodium Chloride, and purified water. The CoVer project was completed from A-Z in just over 6 months. GMP standard operating procedures and processes were developed, and Phase 1 clinical material was manufactured in a sterile ISO class 5 certified flow hood in an ISO class 7 certified clean room. The manufactured product passes sterile criterion for bioburden and microbial limits. This was quite a feat for a start-up company. I truly believe no other company could have created this program and product in the same time frame and yield good Phase 1 clinical results. The project awaits funding to proceed in clinical trials.