| THE FOLDER |

DRUG DEVELOPMENT POST-PANDEMIC: ACCELERATING COVID-ADJACENT CANDIDATES

The COVID19 Pandemic has dealt many changes that have varied from the 'status quo' of drug development and, in my opinion, will have both positive and negative ramifications on this industry for near and long term potential products.

Having joined the Biodextris team in the past couple of years, to manage their marketing and business development activities I have embarked on an exciting ride, especially considering I joined a few months prior to the pandemic! Biodextris is a Canadian, intermediate sized and respected CDMO that **offers process and analytical development services along with manufacturing to early clinical stage material in the biologics sector, for clients across the globe.** Over the past two years, we have been challenged to adjust, realign our business model, and grow to best accommodate our existing clients while taking on **new and pandemic relevant projects** as well! In this period I have made some interesting observations and witnessed trends that are both positive in some aspects and negative in others.

As with the World news, and our lives, over the past couple of years, the research and **drug development sector** has been inundated with activity around COVID19. If one takes a critical assessment of the pandemic period and its impact on drug development, it's likely we will find number of holes to be filled. Interesting enough, there have been many examples where **drug discovery firms made quick pivots** to their development strategy, taking a drug candidate to IND via a COVID related indication even though an initial indication was targeted towards something else (symptomatically related but not specific to COVID19), such as a cardiovascular or pulmonary dysfunctions, for example. The philosophy is that if the drug can be passed through the system quickly and get government support for the process development and preclinical safety related testing, then filing another indication will be a lesser task, both in process and cost, post pandemic.

At Biodextris, we have engaged in many such drug development projects, and in order manage the load, started running parallel activities, extending the workday, and even, sharing portions of work between our sister organizations in order to **meet rigorous timelines in the rush to produce clinical materials.** Our weekly activities are tightly intertwined with various parts of the Canadian government, who have contributed greatly in both funding as well as manpower and expertise, with the express goal to **end the pandemic and build Canadian resources.** Below, we have highlighted a couple of these organizations and the basis of their products to illustrate these highlighted types of projects.

ACE2 Receptor related Therapies (cardiovascular and pulmonary)

With all the intense study around **the ACE2 membrane protein and processes,** due to COVID19, the World has a lot of new data to sift through which may be put to use in drug development. Previous, as well as recent research has indicated the ACE2 receptors/proteins are found in the surface membranes on alveolar (lung) epithelial cells and capillary endothelial cells as well as being highly expressed in many organs such as kidneys, gut and **brain**[1], as one might notice tissues rich in capillaries. The ACE2 receptor

system is very important for a variety of homeostatic systems in the human body related to hypertension (blocks ANG II protein effect, a vasoconstrictor) and in fact mouse models made without ACE2 expression clearly illustrated other systems with pathologies like "cardiac systolic dysfunction, increased blood pressure, myocardial interstitial fibrosis, endothelial dysfunction, and exhibit increased susceptibility to intravascular thrombosis, chronic kidney disease, metabolic abnormalities, and various other biological abnormalities"[2]. Ironically, **COVID19 wreaks havoc on these very systems** often causing cascades of ill effects that eventually could compound and lead to long term injury or death. All that said, there are several health conditions like diabetes, AKI (acute kidney injury) and ARDS (acute respiratory disease) that can be the result of existing conditions other than COVID19. As such there are various ACE2 Receptor-related Therapies rapidly coming to market to address these conditions above and may arrive under COVID19 expedited funding and time conscious regulatory framework but will eventually make a positive impact in these diseases. Drug development of **one such therapeutic called JN2019** whose path to commercialization is being steered by **JN Nova**[3].

Biodextris is currently engaged in aiding JN Nova with the process development while recognizing past candidate development and current assistance from the Canadian government both financially and supportively. This is merely one example within Biodextris itself, and of course one of many that are afoot across the globe.

Cancer therapeutics

Cancer therapeutics and treatments have been the topic of conversation in most major hospitals around the World during the pandemic as there have been many procedures and treatments cancelled in order to triage COVID19 patients and prevent the further spread of the virus. Further, there has also been a reluctance to go, in emergency situations or even at least for critical diagnostics processes in the first place, as people try to avoid the hospitals or well populated facilities[4]. The result will be many previously undiagnosed patients flooding the system as well as patients in various stages requiring treatment, clearly 'COVID19 related' collateral damage. There are several new promising biologic molecules in development as well as **some non-traditional 'whole cell' type therapeutics called SSIs** (site specific immunomodulators) like **QBKPN, being developed by QuBiologics**[5], and has already been used successfully in a 'compassionate use' application in cancer patients! Society will need to rely on next-generation solutions through drug development of cancer therapeutics to help us catch up on lost time.

As for the aforementioned negative affects of the pandemic, the resources and pace that was allocated to the COVID19 efforts has left many **non-COVID projects waiting for a path to commercialization.** In an effort to ameliorate the situation, The Clean Biologics family of companies has been doing its best to assist our COVID19 related projects in an expedited manner, to help our clients 'round the bend' in their clinical trials and final commercial batches, but we have also kept other projects moving as well. We also starting to see **the wave of delayed non-COVID projects, such as cancer therapies, coming back online** and many inquiries about our services. All of our teams are ready to take bookings but certainly are encouraging our potential clients to try and book as early as possible to lock in their slot as the volume of work is still intense. We recommend engaging with your CDMOs as soon as possible to get a barometer on workloads as many new clients are surprised that openings are currently several months or possibly more across the industry.

The Clean Biologics Group

- Clean Cells: Offering an extensive range of services including **safety testing of bipharmaceuticals, cell and virus banking in GMP setting and secured storage of GMP and non-GMP material.** Clean Cells aims at playing a key part in the drug development of innovative therapies and in the emergence of personalized (or precision) medicine.
- Naobios: CDMO ("Contract Development and Manufacturing Organization") **performing process develoment and GMP manufacturing of preclinical and clinical lots** of viral vaccines and viral vectors.
- Biodextris: The newest addition to the team, a CDMO offering expertise in **process and analytical development as well as GMP manufacturing** of a wide array of biologics from drug candidate to clinical material

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