C1: HOW THE C1 PLATFORM WILL CHANGE THE PRODUCTION APPROACH FOR THERAPEUTIC PROTEINS

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For over 30 years, Dyadic has proven itself, both commercially and scientifically, to be a high quality and highly productive producer of enzymes and proteins for specialty chemical applications using a proprietary and patented expression system based on the *Myceliopthora thermophila* fungus, nicknamed C1.

The C1 platform technology, a hyper-productive fungal expression system, was used to develop & manufacture large quantities of desired proteins at industrial scale at significantly lower capital and operating expenditures. In this presentation we shall demonstrate how the benefits of C1 as a successful production host is now being harnessed by Dyadic to produce biological medicines and vaccines.

Using new and improved C1 base strains along with better molecular genetics tools that have been developed over the past several years, we demonstrate the ability of C1 to express mAbs that are secreted, folded correctly and reach high yields. MAbs produced in C1 have almost identical binding kinetics to mAbs produced using CHO cells. In addition, our research program includes comprehensive approach to identify and knock-out proteases for further enhancing protein stability and improving yields.

We have also achieved encouraging results, knowledge and experience in the rVaccine space from our prior research collaboration with Sanofi Pasteur to express rVaccines against Influenza virus. Results of a mice test that was conducted by Sanofi Pasteur, clearly demonstrated that HA produced by C1, generated high immunogenicity response against the virus without any adverse affects.

Like other filamentous fungal strains, C1 has high mannose glycoform structures. However, unlike most fungi and yeasts, C1 does not have ‘high’ mannose (branched 30-50 mannose species), but rather has ‘oligo’ mannose structure (branched 5-9 mannose species). In addition, no O-glycosylation has been observed on C1 secreted proteins, in contrast to *Pichia* that O-glycosylates all secreted antibodies, necessitating deletion of the O-glycosylation machinery. Using the benefits of those advantages, we have started Glycoengineering program aiming to develop C1 strain that produces proteins with defined human-like glycan patterns. The progress we have already made in C1 glycoengineering will also be presented.

Thus, Dyadic firmly believe that the C1 strains that we are developing with offer certain competitive advantages over other leading pharmaceutical expression systems, such as CHO cells, has the potential to become the production system of choice for therapeutic protein and vaccines manufacturing.