Quantoom Biosciences

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How Can Ntensify™ Help with Your mRNA Production Scale-Up?

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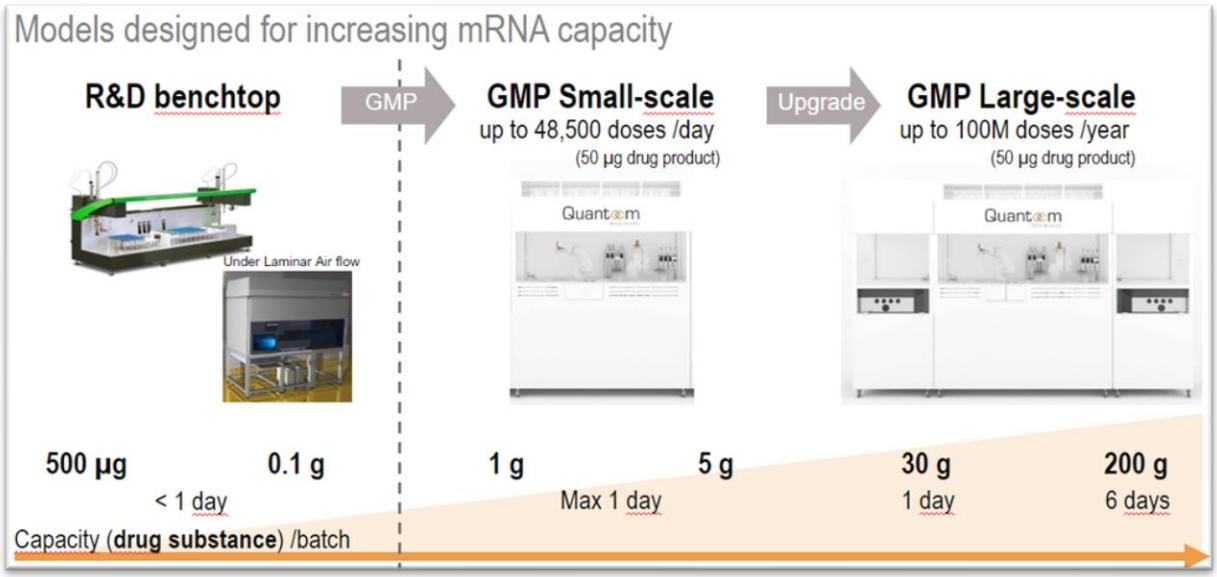
Manufacturing challenges: mRNA vaccines have come a long way since COVID-19; however, production means still have room to improve to meet the growing demand for these novel therapeutics. When observing mRNA production, scaling up requires process development and successive investments in capacities to match larger volumes. Purification is typically lengthy, requiring multiple steps, hence decreasing yields.

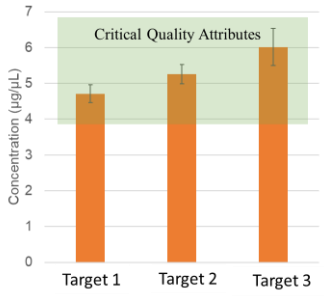
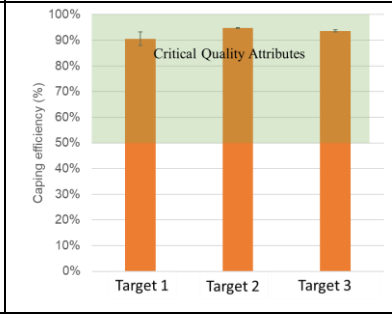
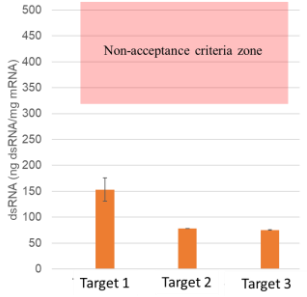
Technology: To address these bottlenecks, Quantoom developed Ntensify™, a solution for mRNA production with three models covering needs from R&D to commercial production. Typically, DNA inputs are fed into the machine, then the template is transcribed into mRNAs, and finally purified, and ready for formulation.



These three models produce different volumes, using the same process. In both GMP-grade production models, the IVT (*in-vitro* transcription) reaction volume is settled on 20 mL. While the small-scale operates in a single batch mode, the large-scale permits the production in repeated batch mode, avoiding adjustments with larger volumes. The R&D benchtop model runs according to the same process, but in smaller volumes using 96-well microplates for screening or pre-clinical purposes.

Optimal Process: The rationale focused on IVT optimisation to minimise complex purification. The IVT process was initially developed and transferred from our partner, eTheRNA Immunotherapies [1]. Quantoom further developed this process to reach an optimal IVT, validated for multiple constructs. To guarantee the best performances, all reagents are available as plug-and-play pre-mixes at the correct concentration and ratio.

Process Performance: The optimised IVT produces high-quality mRNAs with yield > 4 µg/µL and efficient capping > 90%. In addition, the double-stranded RNA contents are < 150 ng dsRNA/mg RNA. Three targets with different lengths were selected: target 1, 2, and 3 have respectively 1189, 4000, and 4284 nucleotides. The CQAs (critical quality attributes) of mRNA are described in literature [2]. These CQAs specifications related to IVT were met for each construct and overshot in the case of dsRNA contents.

Bar graph of mRNA yields	Bar graph of capping efficiencies	Bar graph of dsRNA contents
		
Critical Quality Attributes were defined internally and are described in literature [2].		

Benefits: While generating high-quality mRNAs, Ntensify™ provides additional benefits:

- guaranteed performances with plug-and-play reagents
- needless process development for scaling-up above 20 mL to accelerate timelines into clinical testing
- lower CoGs thanks to higher yield of purified mRNAs
- fully automated (from IVT to purification) for ease of use
- low footprint facility thanks to the integration of numerous steps and simpler purification

The Ntensify™ technology is part of a larger platform called Nfinity™ offering seamless production starting from DNA template to encapsulation in lipidic vehicles.

Further developments aim to validate the system for self-amplifying RNAs.

References:

1. Quantoom Biosciences, 29th June 2021, "*eTheRNA Immunotherapies and Quantoom Biosciences Announce a Strategic Collaboration for the Development of a Novel RNA Production System"*, Link
2. Daniel S., *et al.*, *Quality by Design for Enabling RNA Platform Production Processes*, Trends in Biotechnology, 2178 No of page 16, 2022