

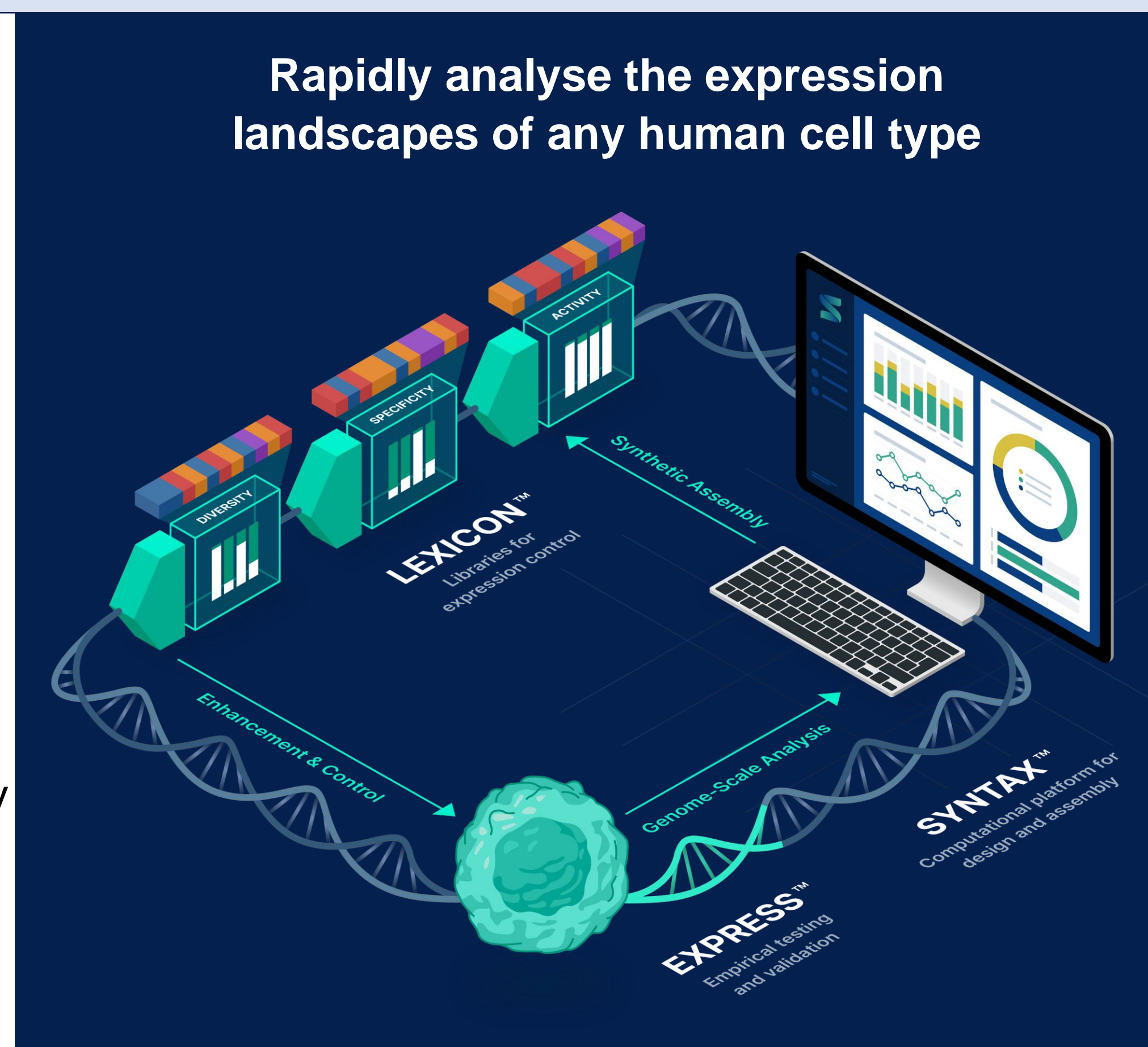
Enabling next-generation medicines: controlling transgene dynamics with synthetic biology

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Engineering expression control

- ✓ **Novel design of synthetic gene expression systems**
 - User-defined requirements
- ✓ **Efficient control of gene expression for tuneable activity**
 - Improve vector efficacy
- ✓ **Precision cell/tissue targeted expression**
 - Reduced toxicity & enhanced patient safety
- ✓ **Minimal length**
 - Increased AAV cargo capacity



SynGenSys platform technology

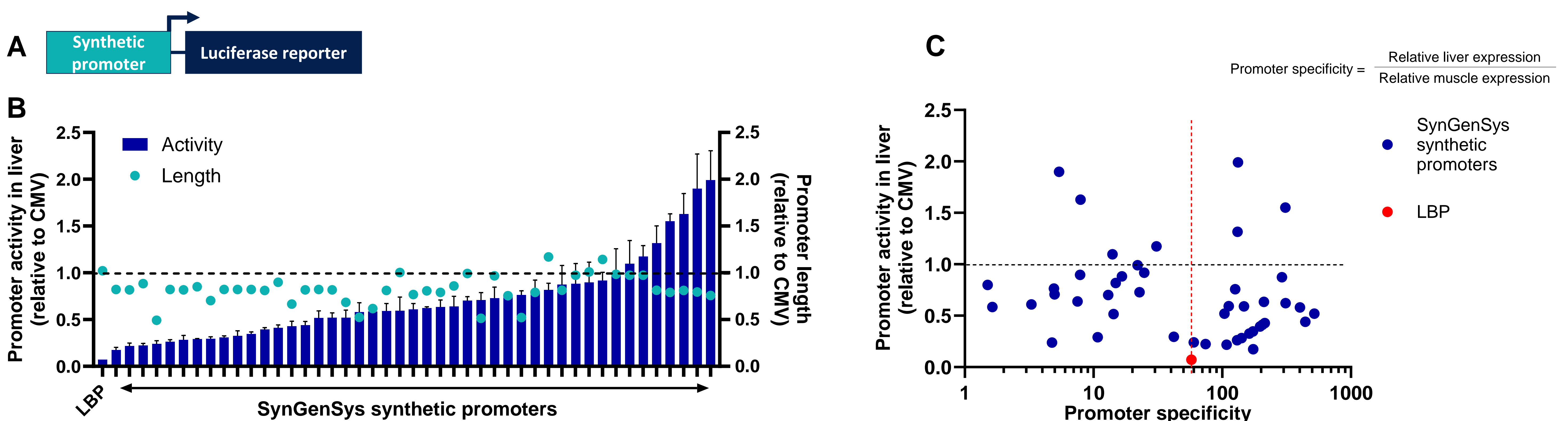
- ✓ **SynGenSys SYNTAX™**: Proprietary bioinformatics platform harnesses streams of **genomic and proteomic data** to design **novel synthetic gene expression systems**
- ✓ **SynGenSys LEXICON™**: Libraries of **curated genetic components** accelerate the assembly of application-specific solutions
- ✓ **SynGenSys EXPRESS™**: **Functional validation in model systems** informs future designs

Novel, synthetic liver promoters - highly tunable and targeted expression at minimal size

✓ Up to **50% smaller** than CMV

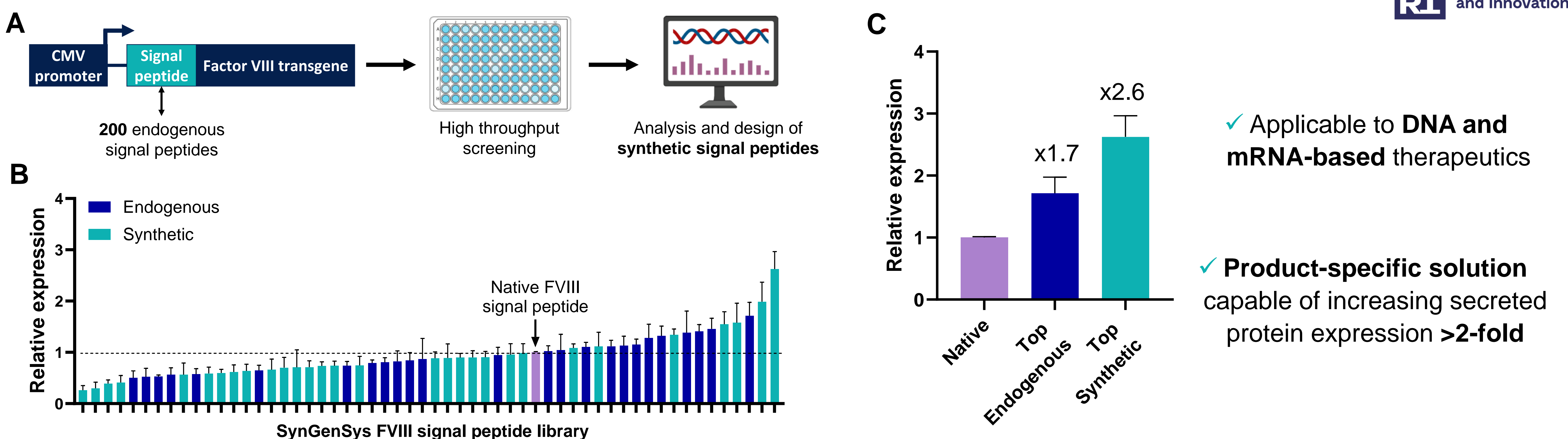
✓ **>10-fold expression range**

✓ **Liver-targeted expression**



A) The constitutive CMV promoter driving luciferase reporter expression was exchanged for liver-targeted synthetic promoters. **B)** 45 SynGenSys synthetic promoters are transiently transfected in the human liver cell line, HepG2, and compared to the constitutive CMV promoter and a clinically relevant liver-specific benchmark promoter (LBP). **C)** SynGenSys synthetic promoters cover a broad range of activity and specificity when compared to the CMV and LBP. Muscle cell line: differentiated C2C12.

Synthetic signal peptides improve secreted protein production



A) The native Factor VIII (FVIII) signal peptide was replaced with 200 endogenous alternatives and screened in the HepG2 cell line for their impact on FVIII expression. Using these results, synthetic signal peptides were designed. **B)** A library of 55 endogenous and synthetic signal peptides tested in HepG2. **C)** Compared to the native signal peptide, the top endogenous and synthetic signal peptides increased FVIII protein production 1.7-fold and 2.6-fold, respectively.

- ✓ **Applicable to DNA and mRNA-based therapeutics**
- ✓ **Product-specific solution** capable of increasing secreted protein expression **>2-fold**

