

ENHANCED SELF-AMPLIFYING mRNA

ENABLES PROLONGED PROTEIN EXPRESSION AND REDUCED CYTOTOXICITY

The opportunity

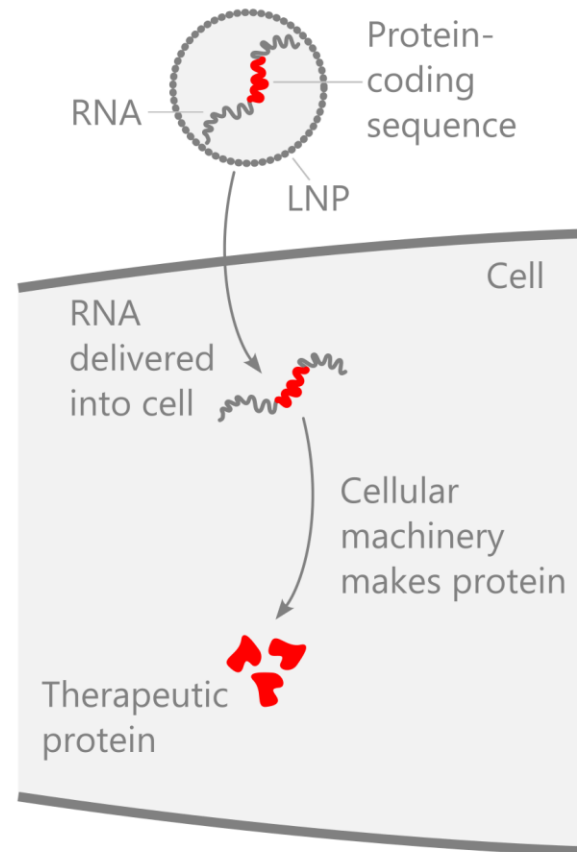
- Need for long-expressing mRNA without toxicity issues

	mRNA	saRNA	eSAM
Expression	<1 week	4-8 weeks	<i>5 months</i>
Cytotoxic	No, if modified	Yes	<i>No</i>
Kinetics	Fast	Fast	<i>Slower</i>

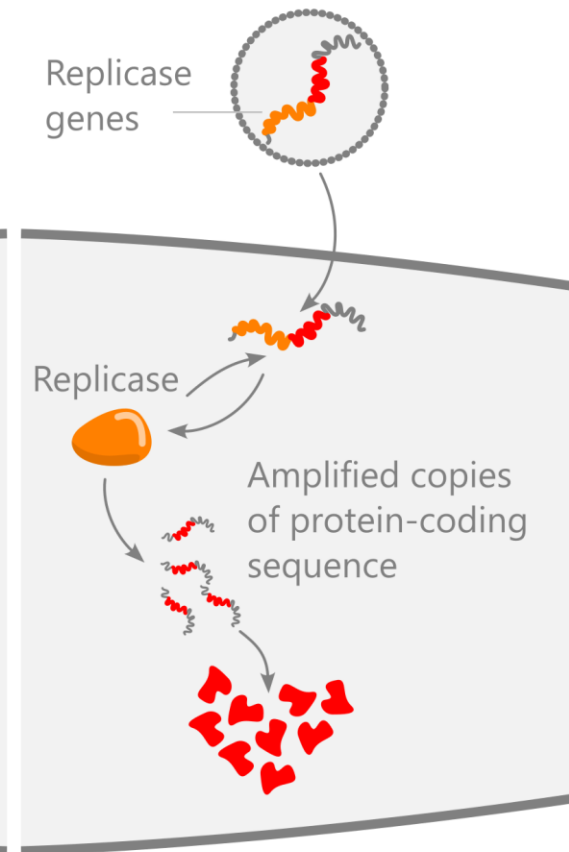
eSAM



Conventional mRNA



Self-amplifying mRNA



Difficulties for saRNA

- Dose-reduction...
 - Flu-like **side effects** as frequent as mRNA, despite 6- to 10-fold lower dose¹

saRNA – dose limitation

“... The 10 µg dose was associated with more local and systemic solicited AE, including grade 3 severity. Although the study stopping rules were not met, the protocol was amended to remove further dose escalation. ...”

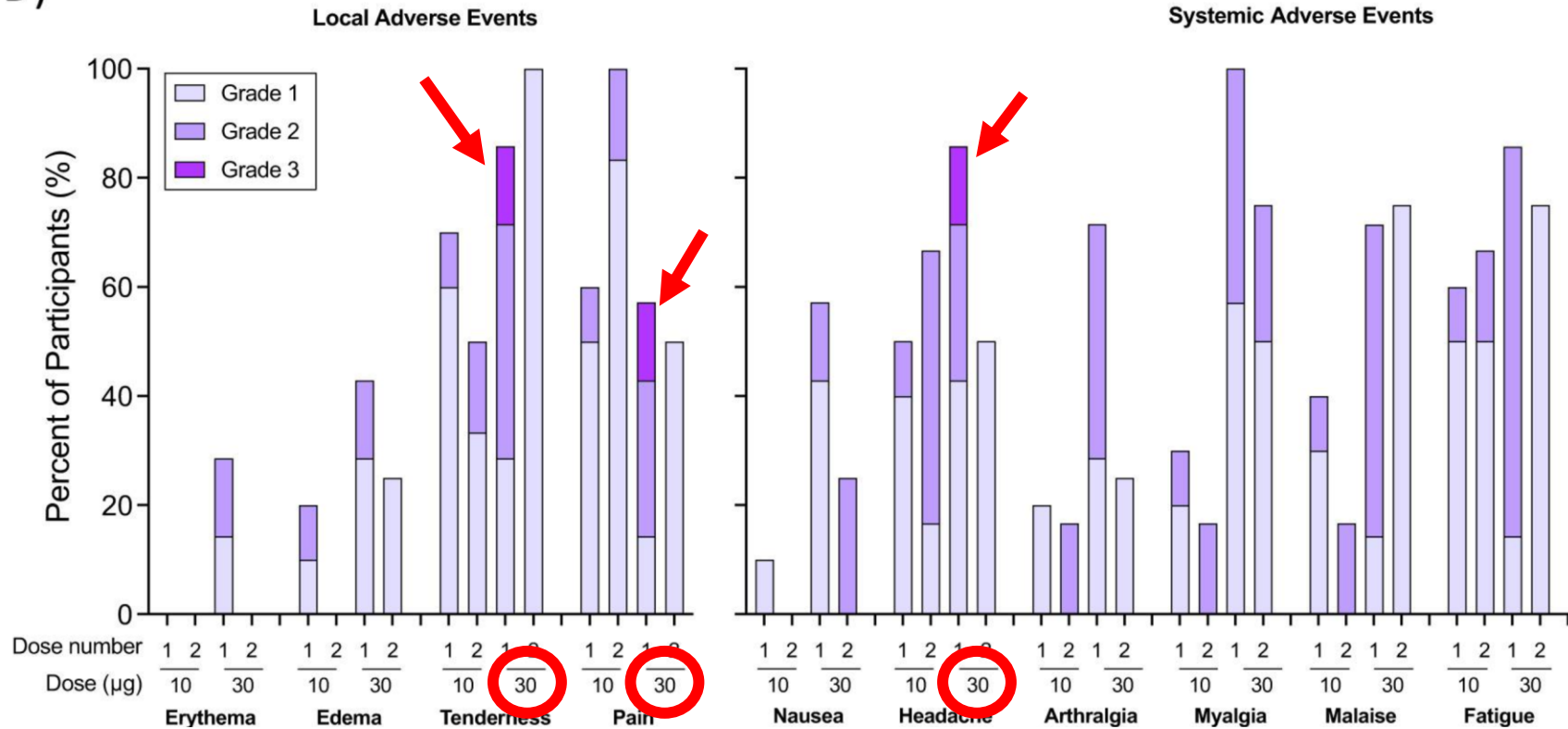
Arcturus Phase I/II Covid-19 vaccine
PMID 36513697

saRNA – dose limitation

“... The proportion of participants reporting a systemic reaction increased significantly with dose reaching 100% of those receiving 5.0 or 10.0µg ($p=0.0001$). Severity also increased with dose and four (17%) of 24 participants who received 10.0µg reported a grade 3 (severe) systemic reaction after the first or second vaccine...”

saRNA – dose limitation

D)



Gritstone Bio Phase I Covid-19 vaccine
PMID 37280238

Difficulties for saRNA

- Dose-reduction...
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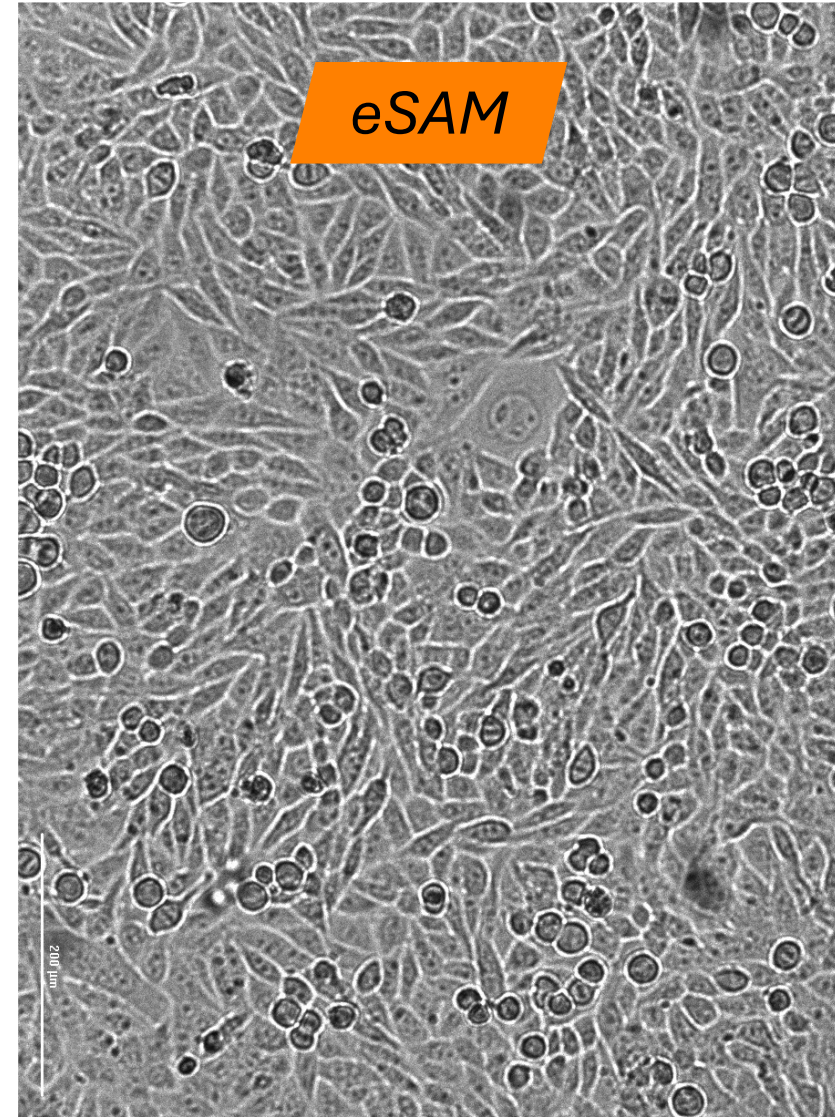
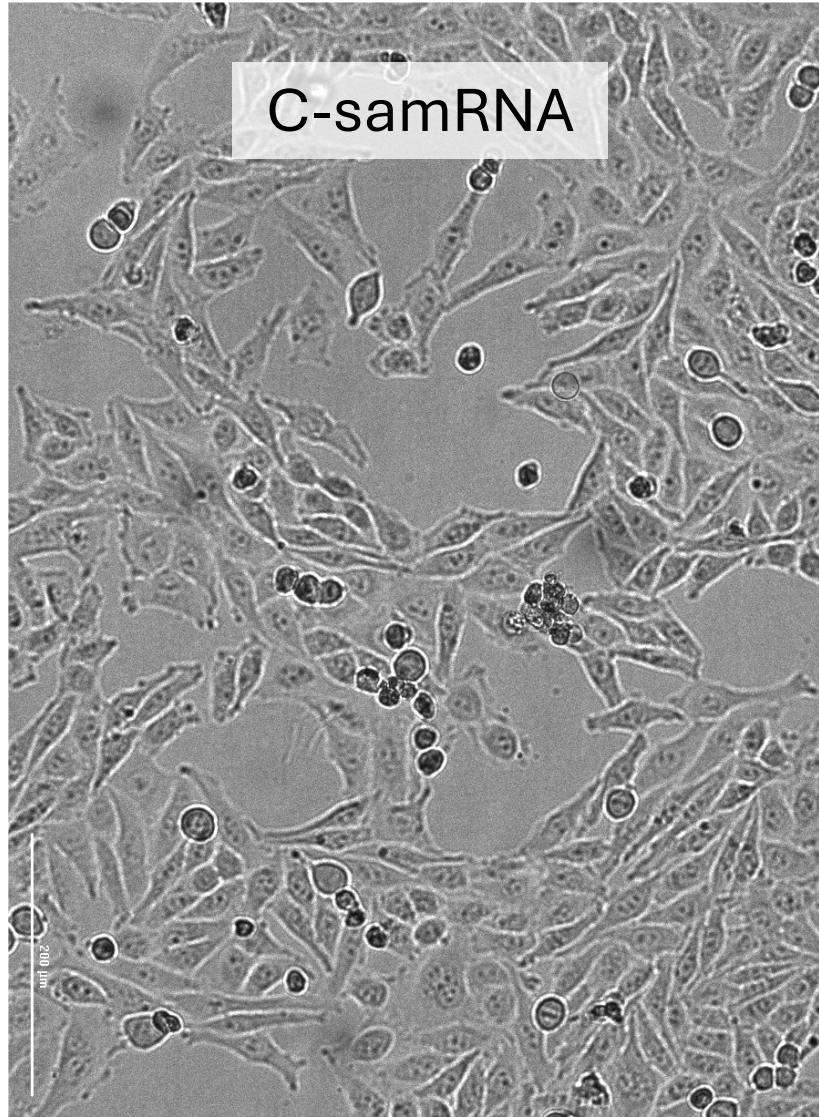
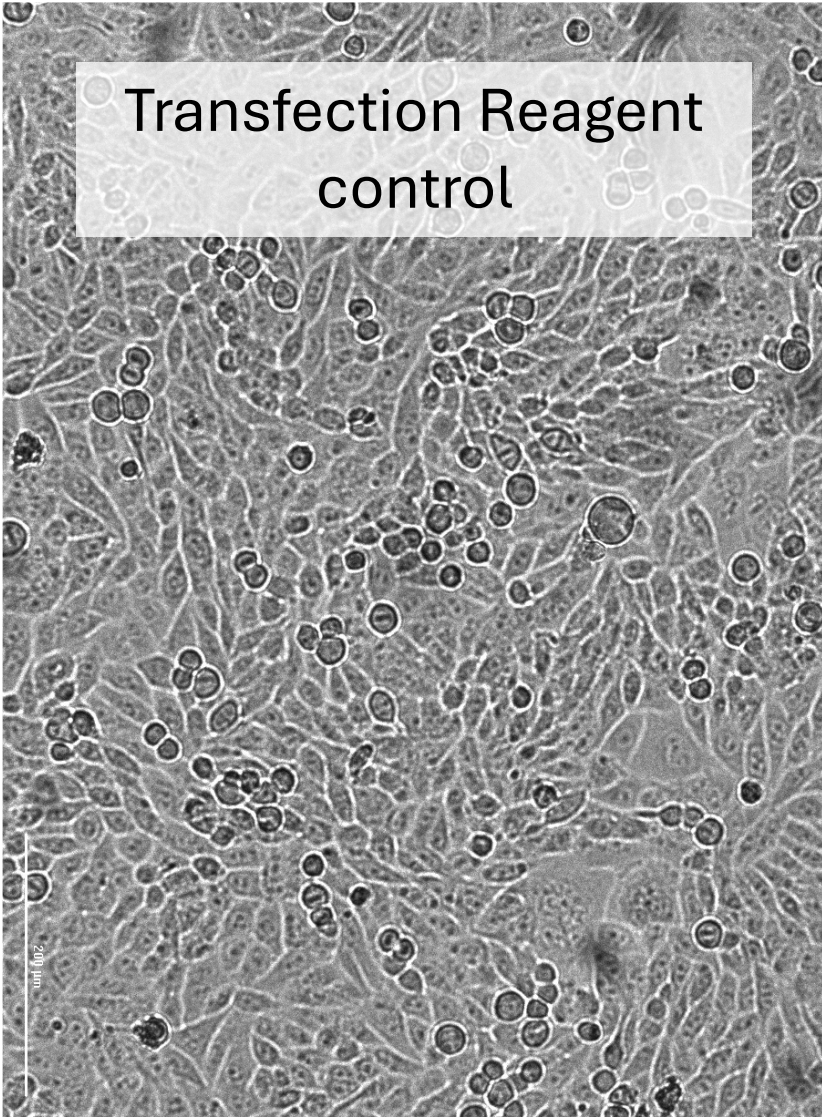
=> Dose-reduction or dose-limitation?

eSAM – reduced cytotoxicity

Transfection Reagent
control

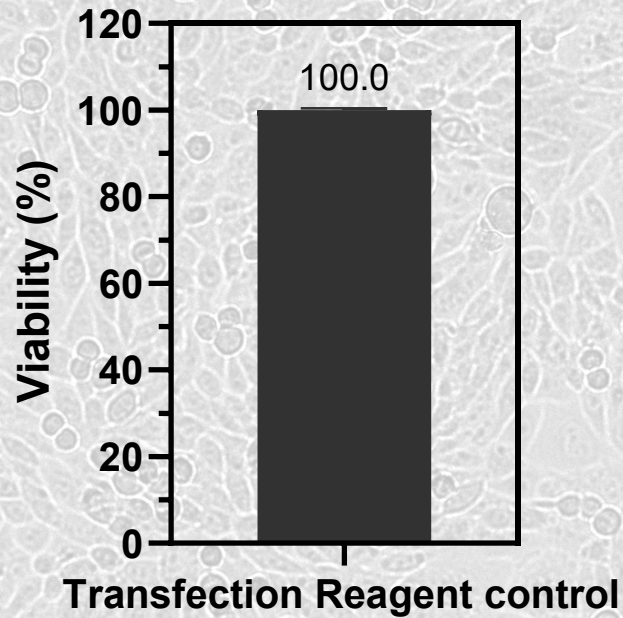
C-samRNA

eSAM

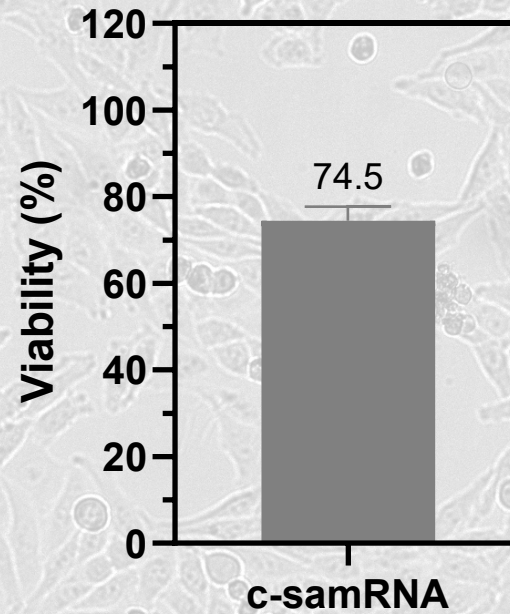


eSAM – reduced cytotoxicity

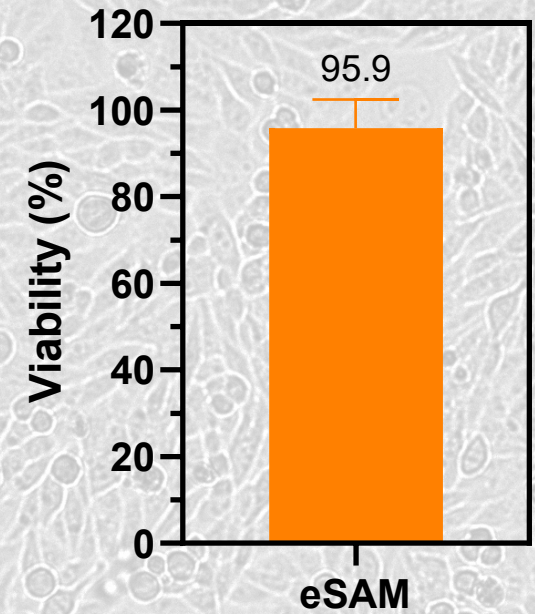
Transfection Reagent control



C-samRNA

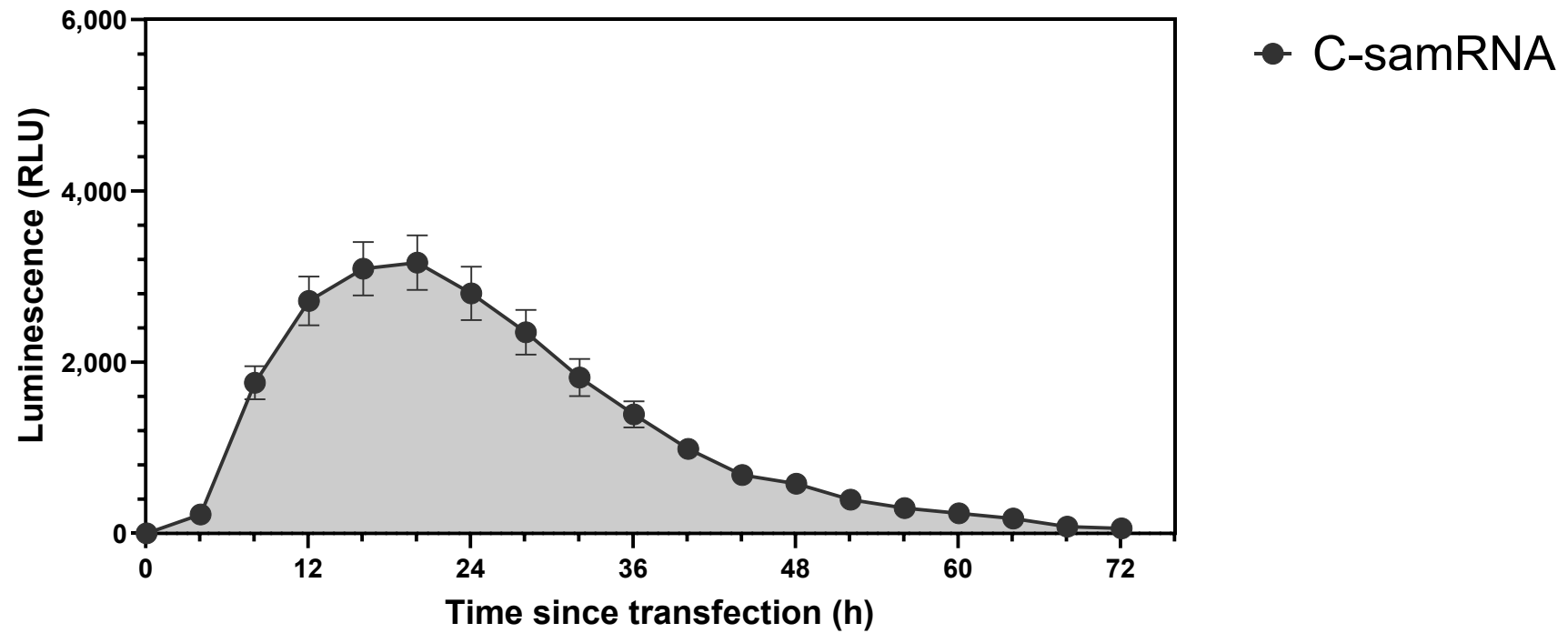


eSAM



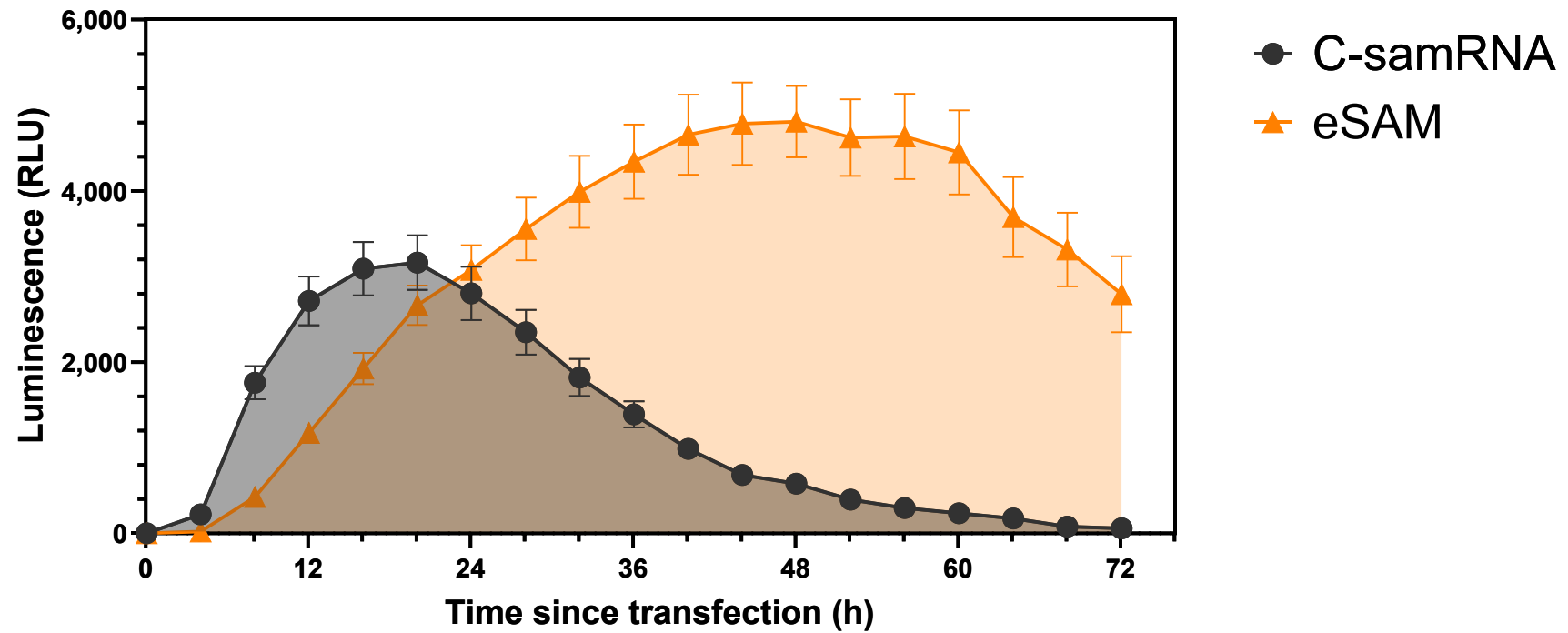
eSAM

eSAM demonstrates altered *in vitro* kinetics

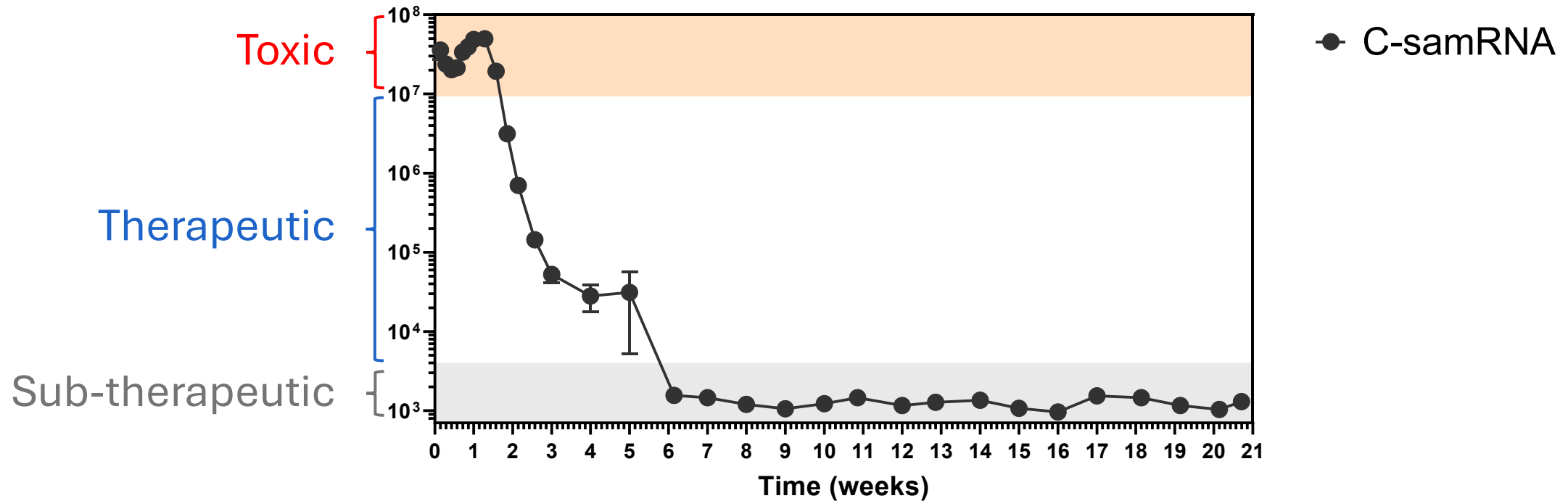


eSAM

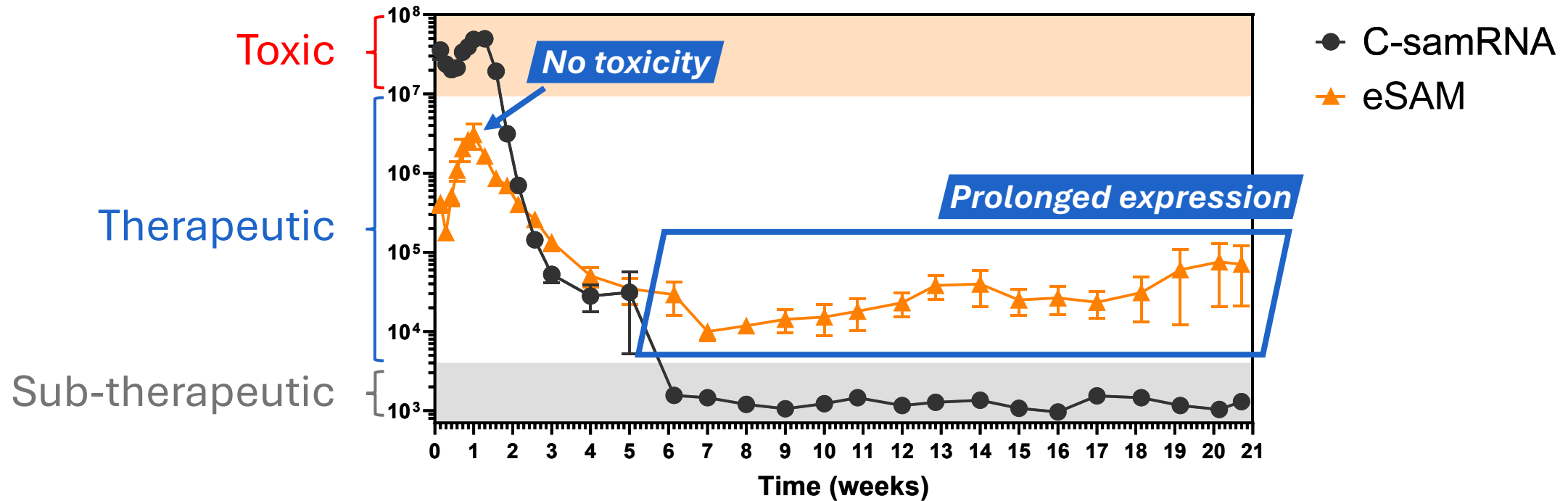
eSAM demonstrates altered *in vitro* kinetics



eSAM – validation of prolonged expression



eSAM – validation of prolonged expression



eSAM – next steps

- Exploring suitable applications
 - For example
 - Vaccination
 - Low-dose immunotherapy
 - Hemophilia
 - Immune tolerance therapy
 - ...
- Safety

	mRNA	samRNA	circRNA	eSAM
Vaccination	+	+	+	+
Cancer therapy	+	+	+	++
Protein replacement				++
CAR-T & stem cells	+	+/-	+/-	?
Low toxicity	+, if modified		+	+
Long-term expression	Days	Weeks	Days	Months
<i>Conclusion</i>	<i>Short expression</i>	<i>Adverse events</i>	<i>Preclinical</i>	<i>Early R&D phase</i>

eSAM – conclusion

- First-in-class new modality
- Multiple potential applications
- Platform family – IP protected through patent

Interested?



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