Dose-Sparing Potential of the Semisynthetic Saponin Adjuvant TQL1055 For Seasonal and Pandemic Influenza

Sean R. Bennett, MD, PhD
Chief Medical Officer
Adjuvance Technologies, Inc.

National Foundation for Infectious Diseases®

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Disclosures

- **Sean R. Bennett** is employed by Adjuvance Technologies, Inc.

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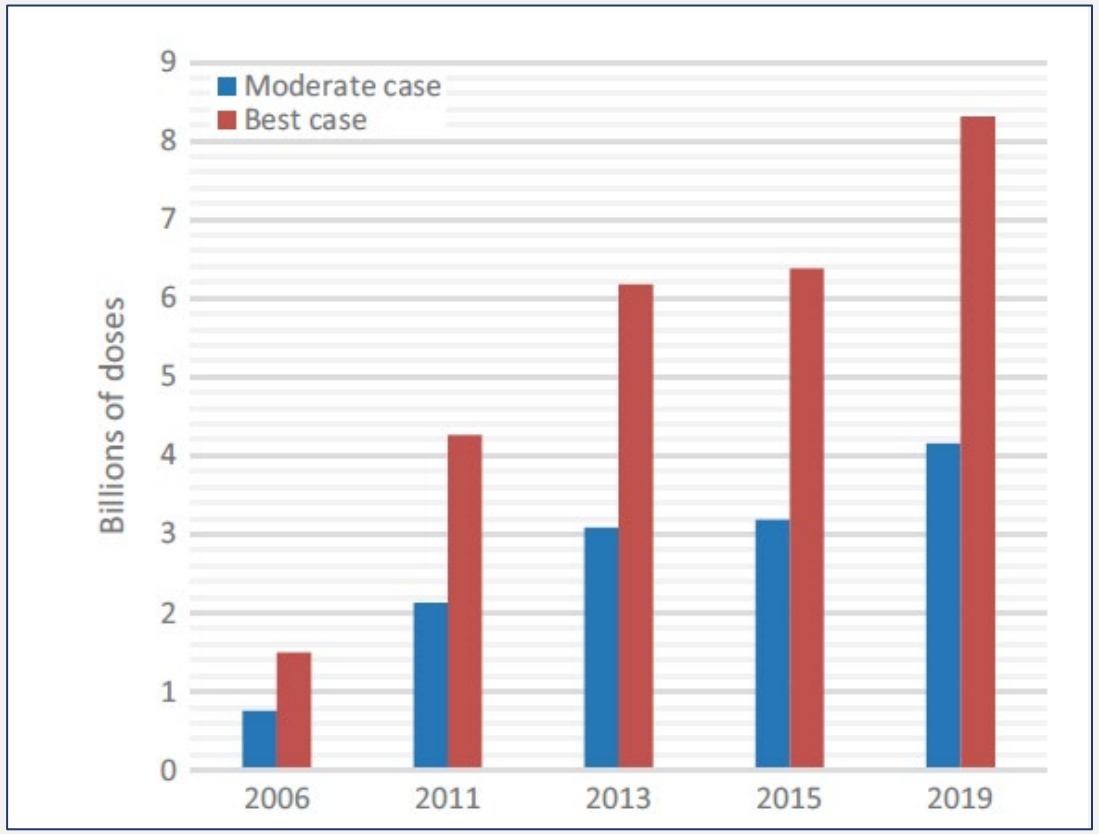
This presentation does not offer CME

Production Capacity: Improving But Still Inadequate

- Novel adjuvants and dose-sparing strategies are essential to achieve adequate global production capacity for both seasonal and pandemic influenza (right)
  - WHO target capacity is 10.9 bn doses
  - Moderate-case production estimate is <50% of WHO target
  - Best-case estimate (assuming 2x dose-sparing) is <80% of WHO target
- Capacity has been strained further by the demands for SARS-CoV2 vaccine production
- Emergence of SARV-CoV2 variants and other novel pathogens may create additional capacity demands

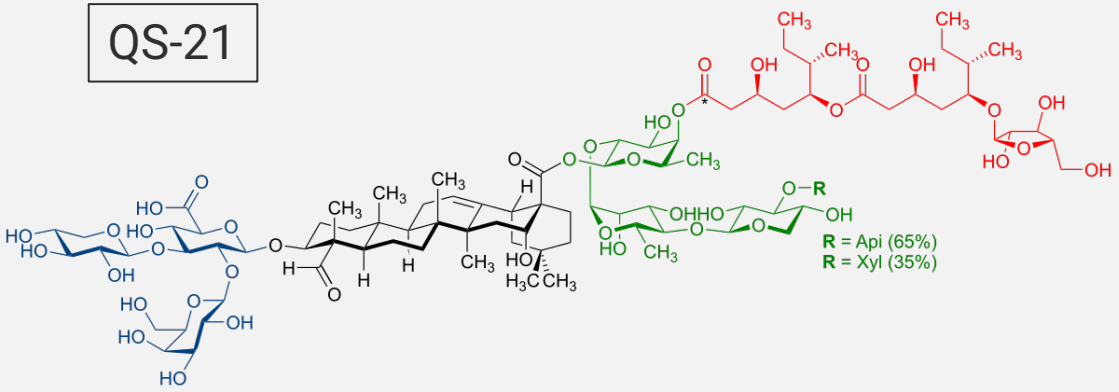


Source: Sparrow E et al. Global production capacity of seasonal and pandemic influenza vaccines in 2019. Vaccine 2021;39:512.

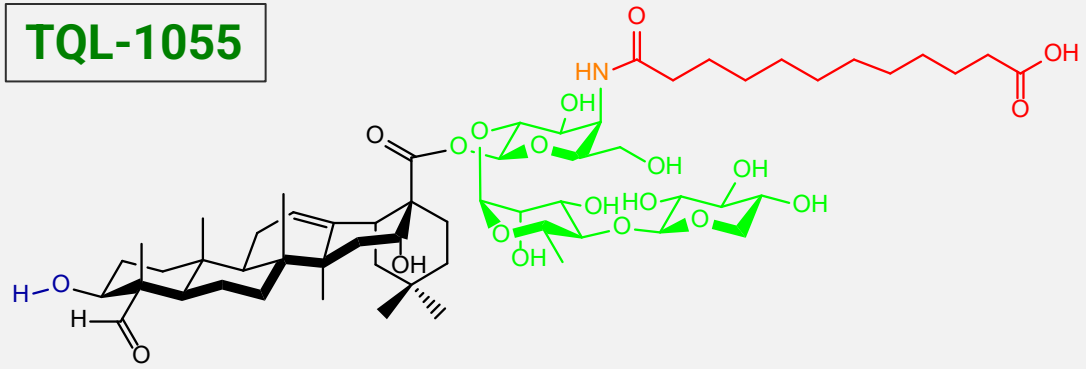
Trade names in this presentation are used for clarification purposes only

TQL-1055: Optimized Saponin Adjuvant

QS-21

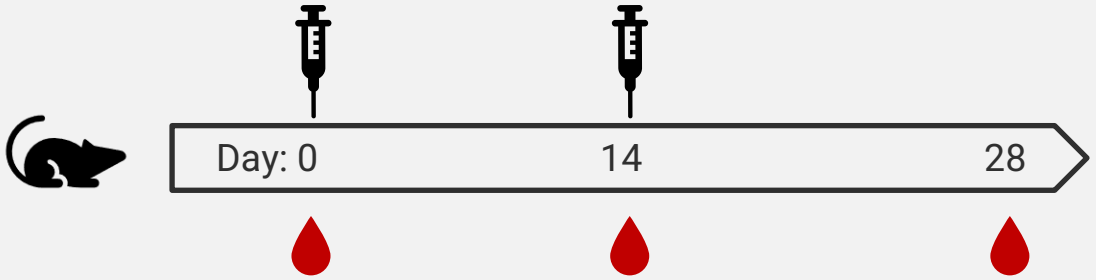


TQL-1055



- Analogue of the natural saponin adjuvant QS-21
- Semi-synthetic; improved supply vs QS-21
- Rationally designed for ease of synthesis and improved stability
- Improved tolerability profile in preclinical studies

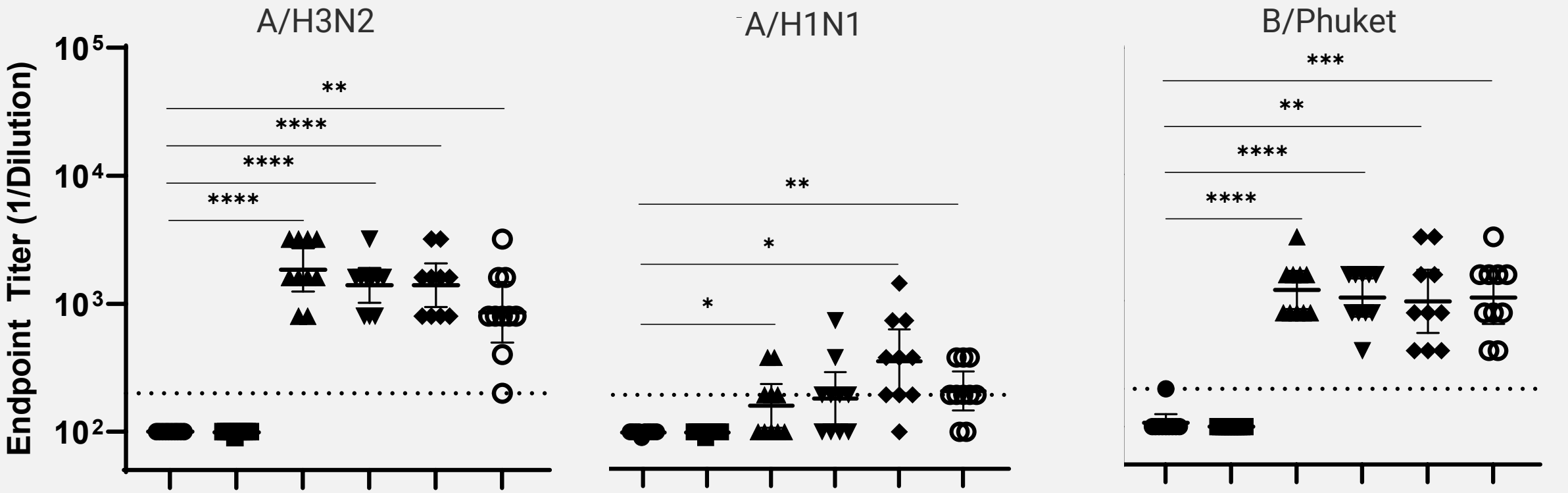
Study 1: Design and Methods



Group	n	HA (per strain), mcg	Dose Reduction	TQL1055, mcg
1	20	4.5	--	--
2	10	1.125	4x	--
3	10	1.125	4x	30
4	10	0.56	8x	30
5	10	0.28	16x	30
6	10	0.14	32x	30

- C57Bl/6J mice
- FluBlok quadrivalent 2019-2020
- Starting dose = 1/10 human dose
- Total HA antigen= 18 mcg
- HA antigen per strain = 4.5 mcg
- Subcutaneous route
- Two-dose series at Day 0 and 14
- Phlebotomy at Days 0, 14, and 28
- Anti-HA IgG ELISA
- Hemagglutinin Inhibition Assay
- Geometric mean titer (GMT) compared by unpaired t-test

Study 1: Anti-HA IgG Titers After Dose 1



Group	1	2	3	4	5	6	1	2	3	4	5	6	1	2	3	4	5	6
HA, mcg	4.5	1.1	1.1	0.56	0.28	0.14	4.5	1.1	1.1	0.56	0.28	0.14	4.5	1.1	1.1	0.56	0.28	0.14
Dose reduction	-	4x	4x	8x	16x	32x	-	4x	4x	8x	16x	32x	-	4x	4x	8x	16x	32x
TQL1055, mcg	-	-	30	30	30	30	-	-	30	30	30	30	-	-	30	30	30	30
GMT	**100**	**99**	**1838**	**1393**	**1393**	**857**	**99**	**99**	**163**	**187**	**373**	**214**	**107**	**100**	**1213**	**1056**	**985**	**1056**
P vs Group 1	nt	nt	<0.0001	<0.0001	<0.0001	0.0017	nt	nt	0.0273	0.0548	0.0102	0.0013	nt	nt	<0.0001	<0.0001	0.0024	0.0003

****P ≤ 0.0001; ***P ≤ 0.001; **P ≤ 0.01; *P ≤ 0.05

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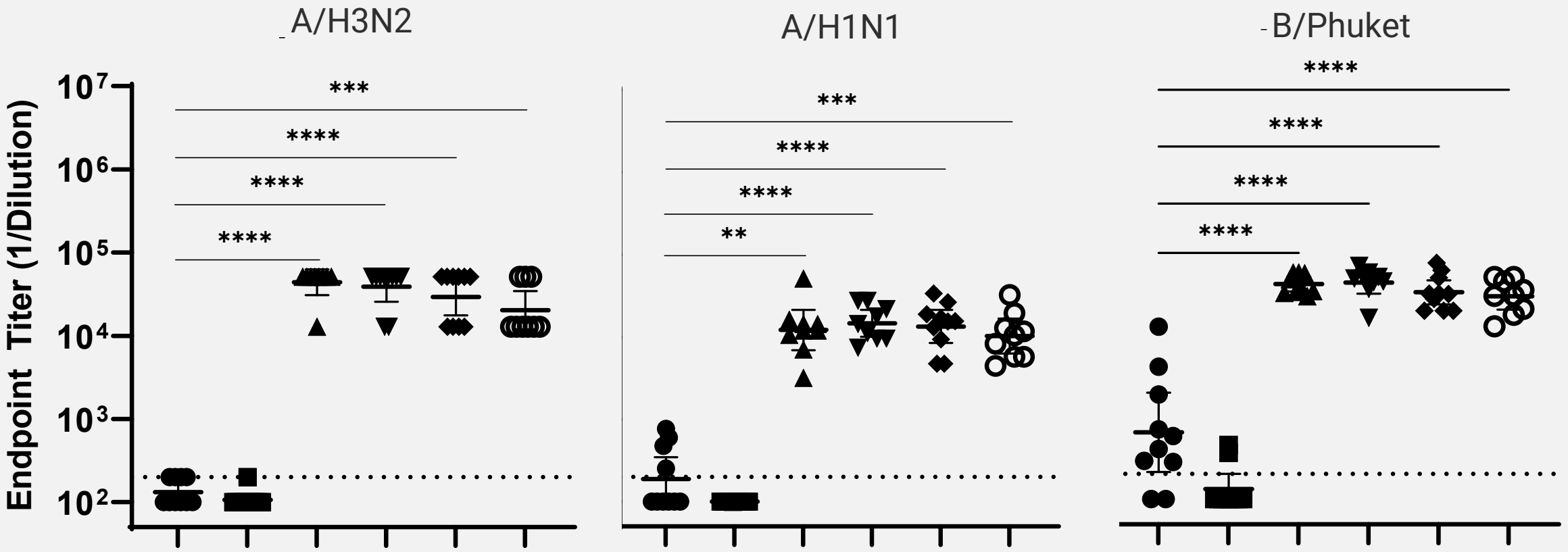
Study 1: Anti-HA IgG Titers After Dose 2



Group	1	2	3	4	5	6	1	2	3	4	5	6	1	2	3	4	5	6
HA, mcg	4.5	1.1	1.1	0.56	0.28	0.14	4.5	1.1	1.1	0.56	0.28	0.14	4.5	1.1	1.1	0.56	0.28	0.14
Dose reduction	-	4x	4x	8x	16x	32x	-	4x	4x	8x	16x	32x	-	4x	4x	8x	16x	32x
TQL1055, mcg	-	-	30	30	30	30	-	-	30	30	30	30	-	-	30	30	30	30
GMT	**132**	**107**	**43891**	**38802**	**29407**	**20319**	**188**	**100**	**12172**	**14678**	**13427**	**10224**	**626**	**132**	**36494**	**38247**	**29174**	**26180**
P vs Group 1	nt	nt	<0.0001	<0.0001	<0.0001	0.0006	nt	nt	0.0026	<0.0001	<0.0001	0.0005	nt	nt	<0.0001	<0.0001	<0.0001	<0.0001

****P ≤ 0.0001; ***P ≤ 0.001; **P ≤ 0.01; *P ≤ 0.05

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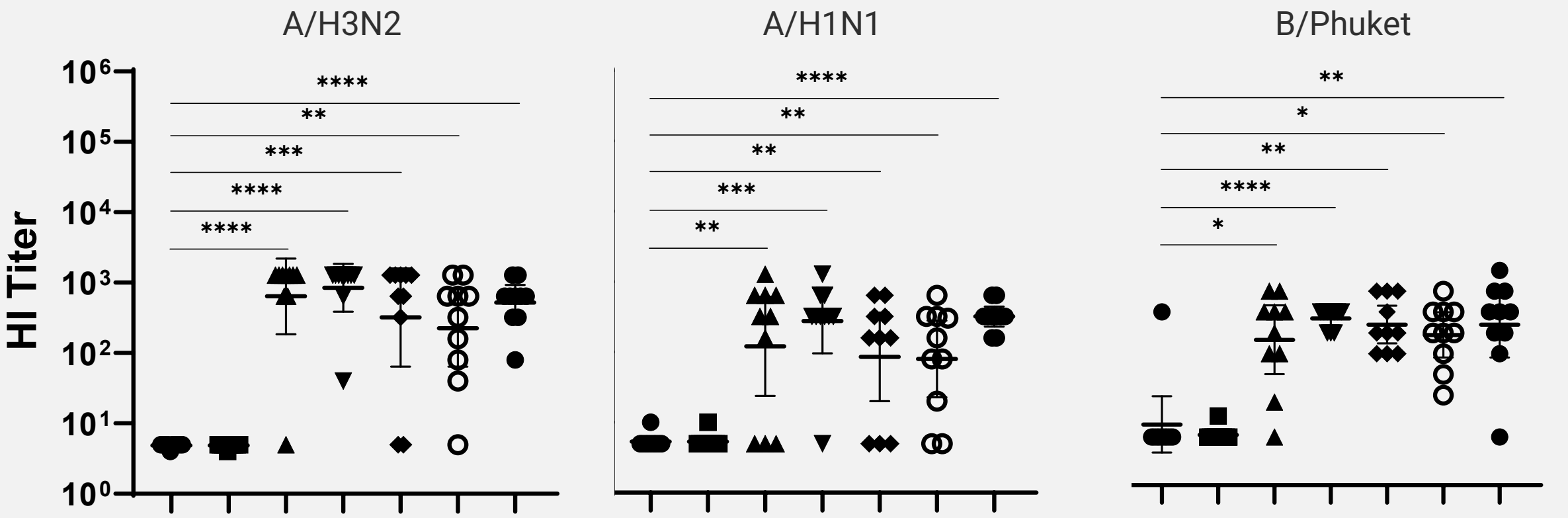
Study 1: Hemagglutinin Inhibition After Dose 2



Group	1	2	3	4	5	6
HA, mcg	4.5	1.1	1.1	0.56	0.28	0.14
Dose reduction	-	4x	4x	8x	16x	32x
TQL1055, mcg	-	-	30	30	30	30
GMT	**5**	**5**	**640**	**845**	**320**	**226**
P value vs Group 1	nt	nt	<0.0001	<0.0001	0.0002	0.0037

1	2	3	4	5	6
4.5	1.1	1.1	0.56	0.28	0.14
-	4x	4x	8x	16x	32x
-	-	30	30	30	30
5	**5**	**121**	**279**	**86**	**80**
nt	nt	0.0064	0.0007	0.0060	0.0091

1	2	3	4	5	6
4.5	1.1	1.1	0.56	0.28	0.14
-	4x	4x	8x	16x	32x
-	-	30	30	30	30
8	**5**	**127**	**260**	**211**	**149**
nt	nt	0.0134	<0.0001	0.0065	0.0121

****P ≤ 0.0001; ***P ≤ 0.001; **P ≤ 0.01; *P ≤ 0.05

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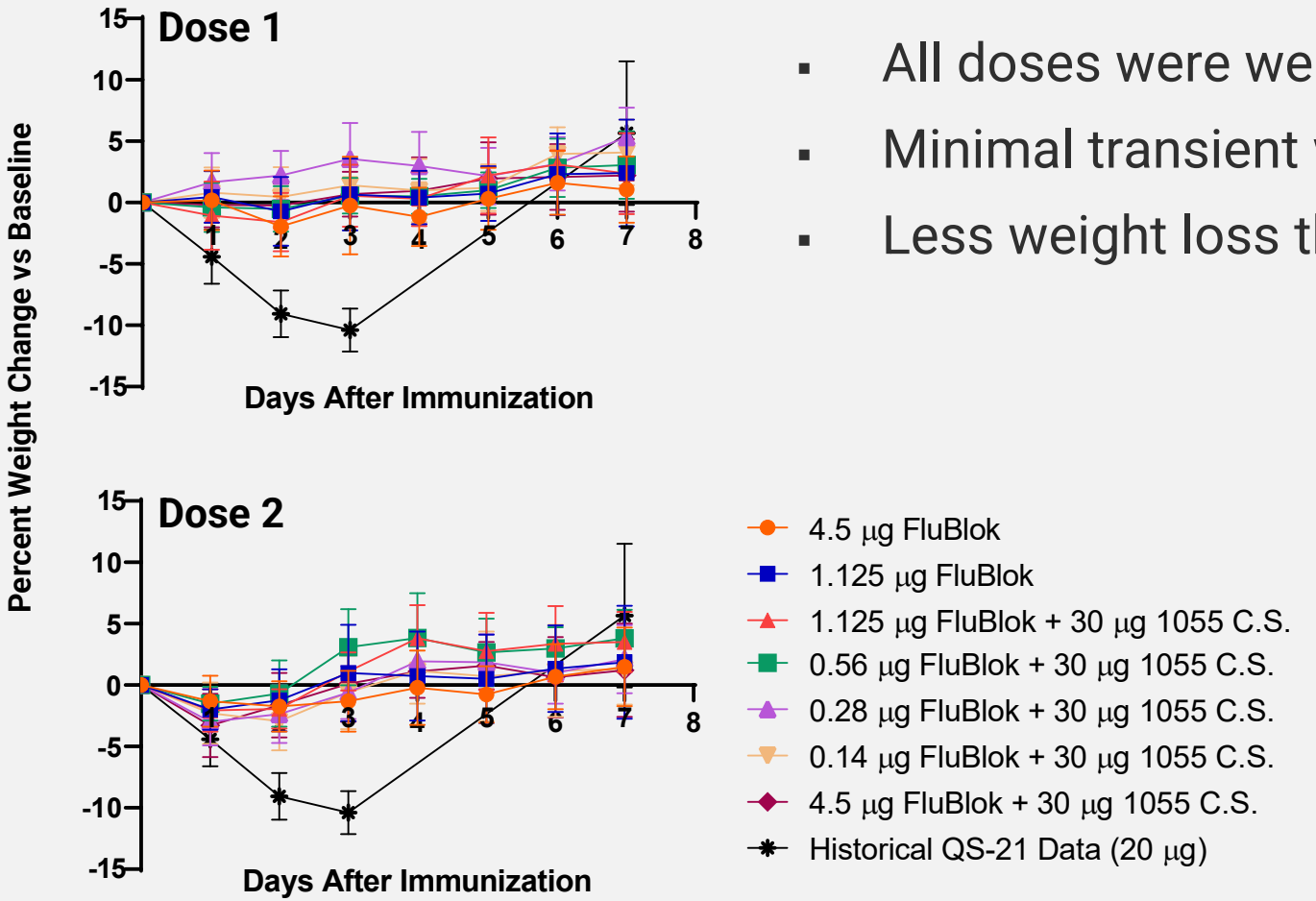
Study 1: Weight Change



- All doses were well-tolerated
- Minimal transient weight loss after dose 1 and dose 2
- Less weight loss than QS-21 after both doses

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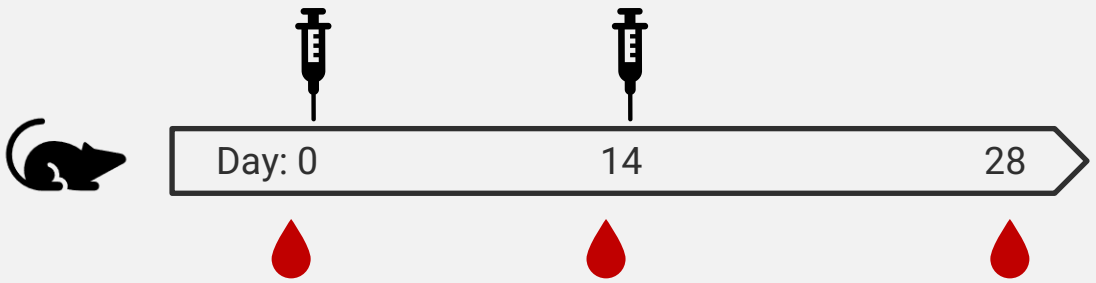
Study 2: Design and Methods

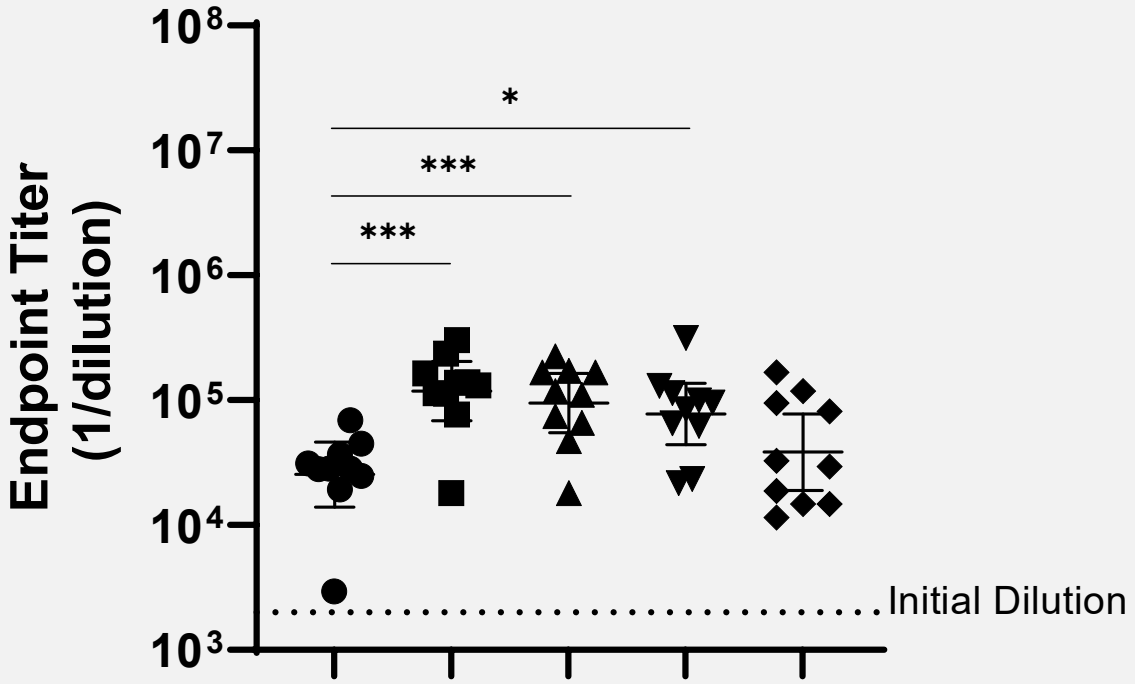


Group	n	HA (per strain), mcg	Dose Reduction	TQL1055, mcg
1	10	4.5	--	--
2	10	0.28	16x	30
3	10	0.14	32x	30
4	**10**	**0.07**	**64x**	**30**
5	**10**	**0.03**	**128x**	**30**

- **CD-1** mice
- Flublok® quadrivalent **2020-2021**
- Starting dose = 1/10 human dose
- Total HA antigen= 18 mcg
- HA antigen per strain = 4.5 mcg
- **Intramuscular route**
- Two-dose series at Days 0, 14
- Phlebotomy at Days -1, 13, 28
- **Anti-HA IgG ELISA (H3N2 only)**
- GMT compared by unpaired t-test

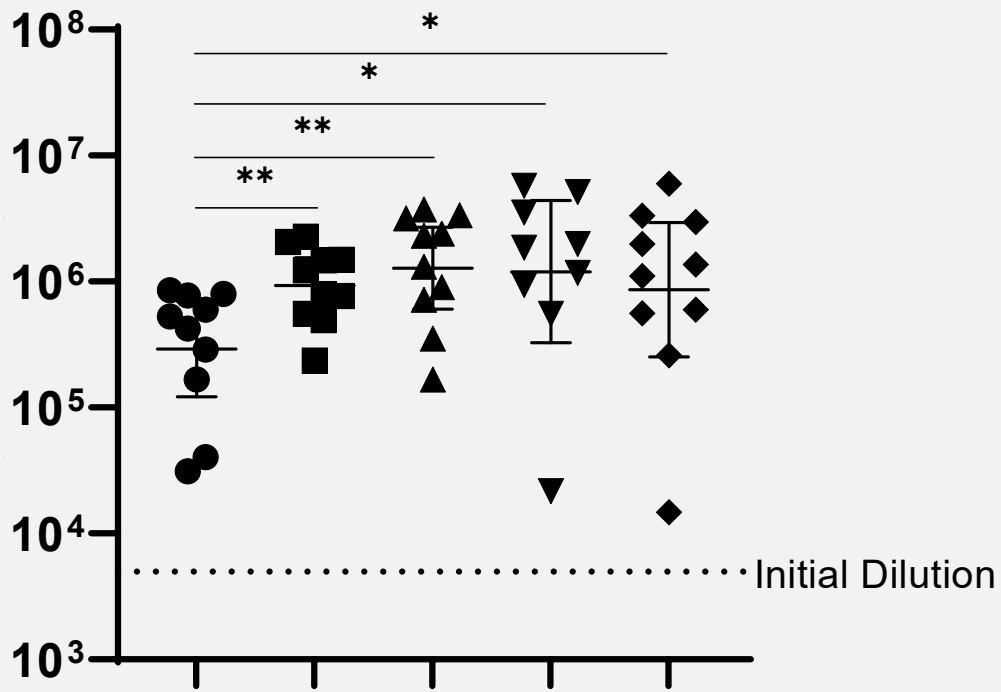
Study 2: Anti-H3N2 IgG Titers

Dose 1



Group	1	2	3	4	5
HA, mcg	4.5	0.28	0.14	0.07	0.03
Dose reduction	-	16x	32x	64x	128x
TQL1055, mcg	-	30	30	30	30
GMT	**25392**	**118118**	**94790**	**77322**	**38392**
P value vs Group 1	nt	0.0004	0.0009	0.0179	0.1497

Dose 2



1	2	3	4	5
4.5	0.28	0.14	0.07	0.03
-	16x	32x	64x	128x
-	30	30	30	30
290627	**932868**	**1276401**	**119751 6**	**861372**
nt	0.0098	0.0044	0.0102	0.0325

****P ≤ 0.0001; ***P ≤ 0.001; **P ≤ 0.01; *P ≤ 0.05

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Conclusions

- The adjuvant effect of TQL1055 was observed for all influenza strains tested
- A robust antibody response was elicited after Dose 1
- There was a >1 log increase in titer after Dose 2
- Similar responses were observed across all antigen doses down to 0.03 mcg (128x dose reduction)
- A functional antibody response was confirmed by hemagglutinin inhibition
- Doses were well-tolerated with minimal weight loss
- Findings were consistent across two mouse strains
- Based on these findings, TQL1055 may be a useful tool to enhance antigen dose-sparing and improve influenza vaccine availability

Acknowledgements

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