Next-generation saponin adjuvant: First-in-human clinical trial results

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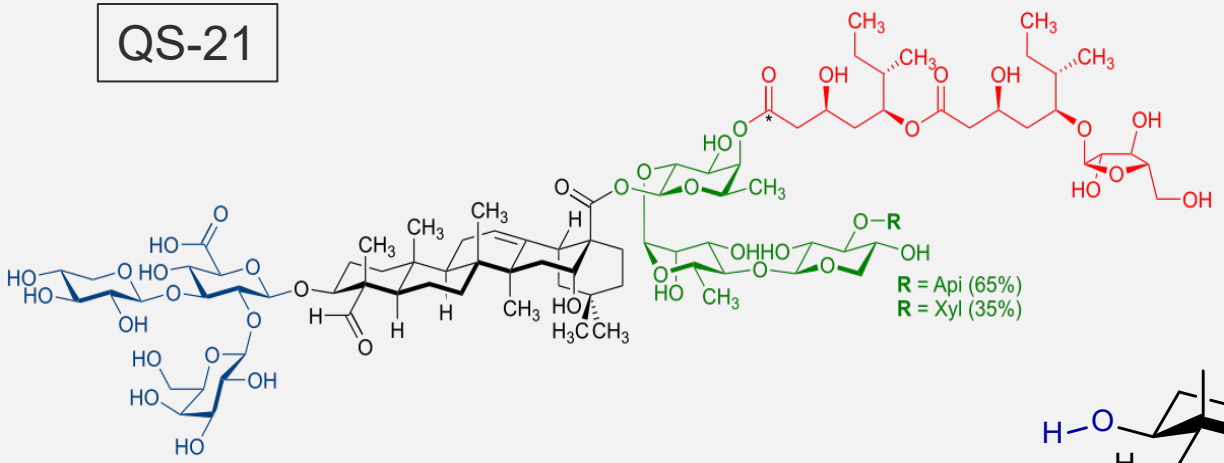
Enhancing Immunity

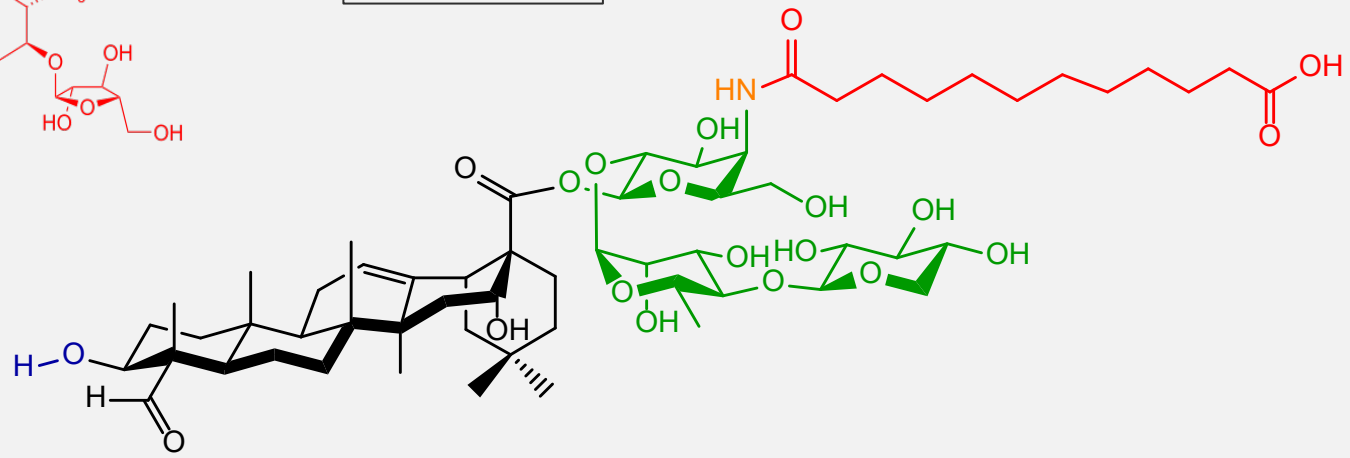
TQL-1055: Optimized saponin adjuvant

- Simplified, stabilized version of QS-21
- Semi-synthetic entity designed to improve tolerability

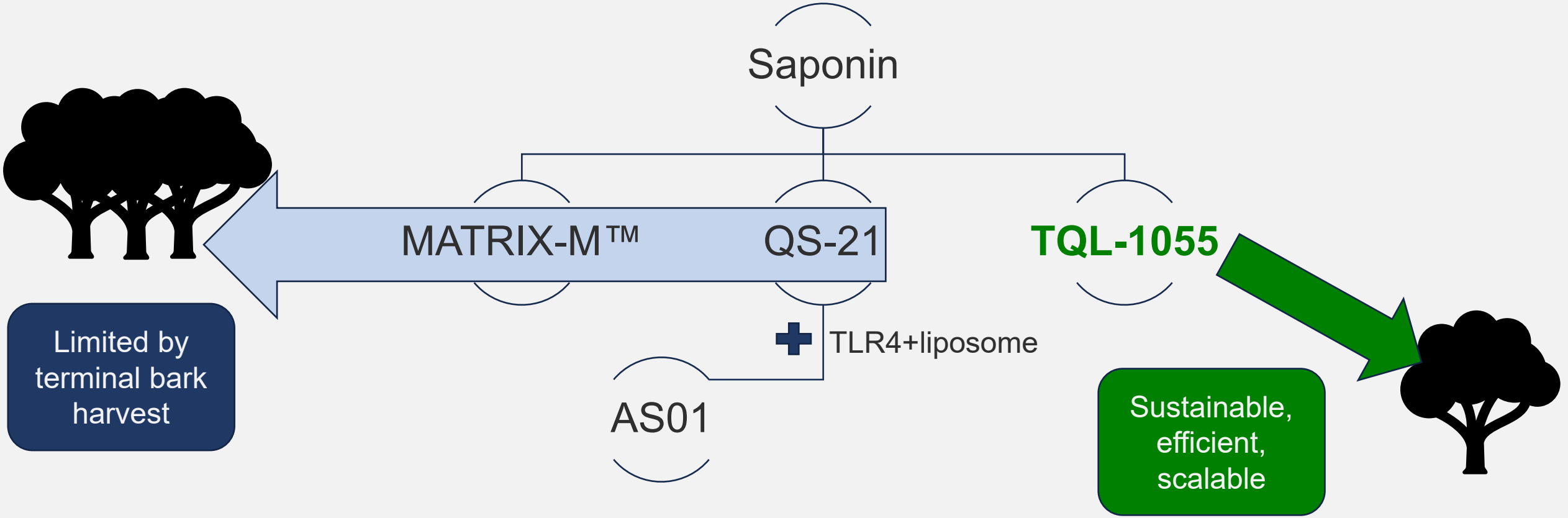
QS-21



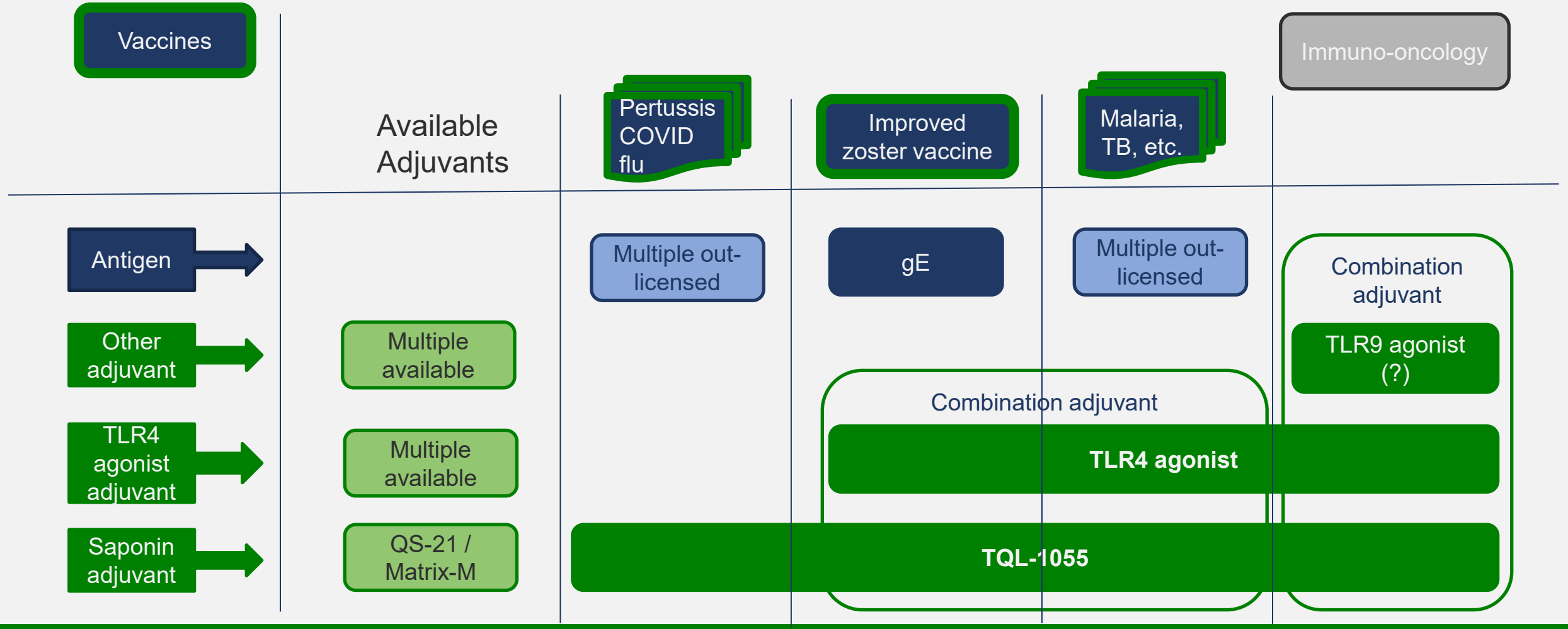
TQL-1055



Sustainability and manufacturing efficiency limits

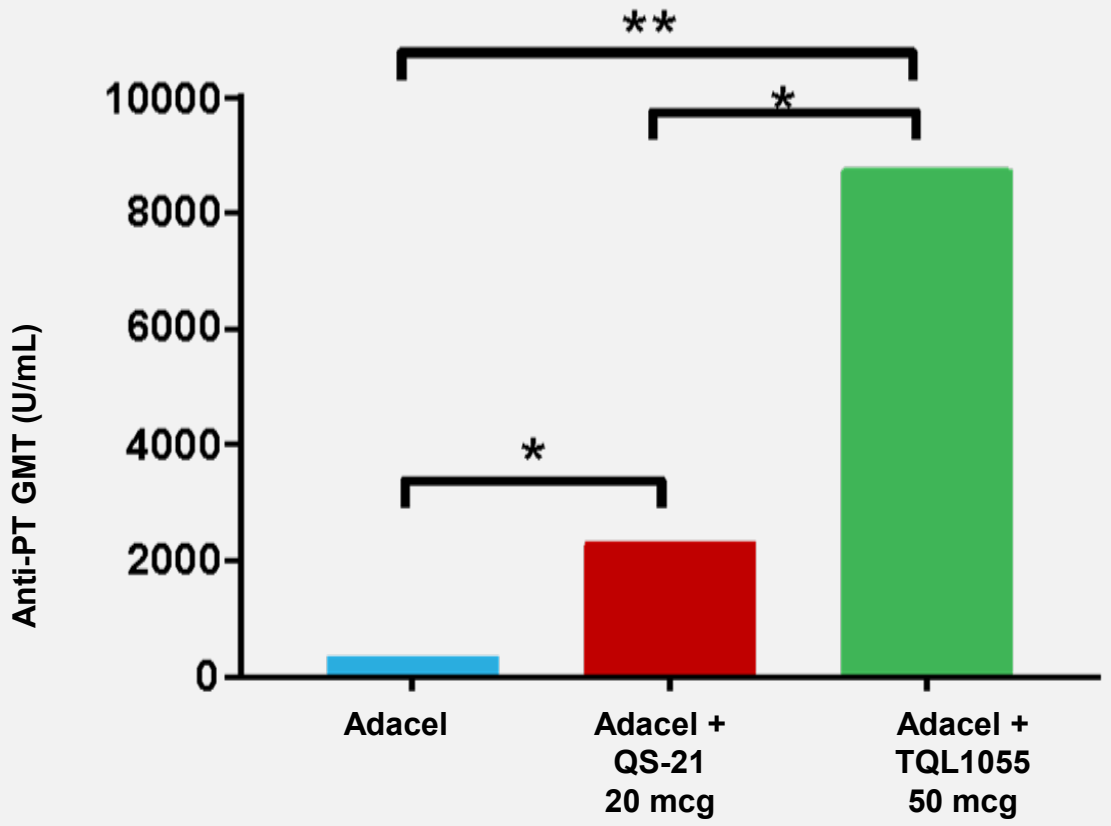


TQL-1055 is the foundation for combination adjuvants



Background: Mouse Immunogenicity

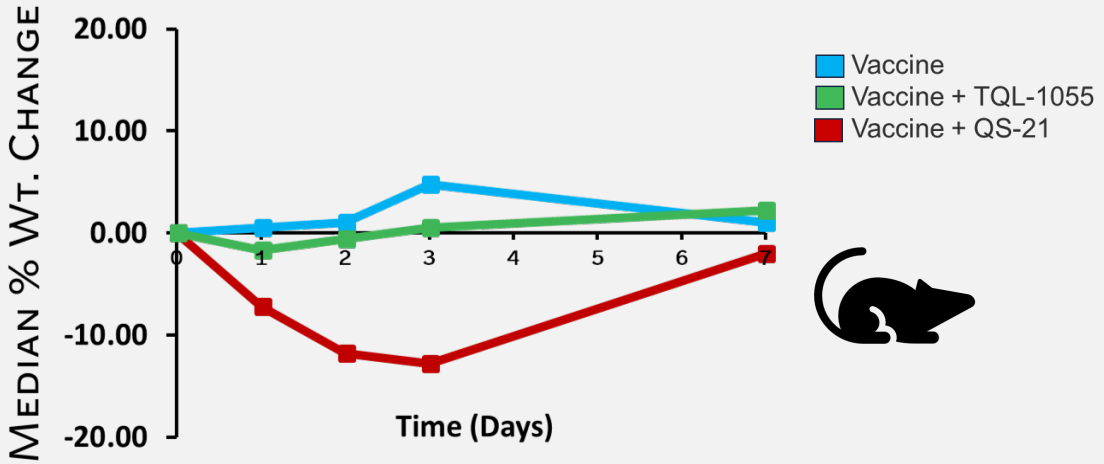
- Pertussis vaccine Adacel + **TQL-1055** generates a higher anti-PT response than either Adacel alone or Adacel + QS-21
- QS-21 exhibits dose-limiting toxicities above 20 mcg
- Confirmed with other pertussis antigens



Background: Improved Tolerability of TQL1055

- Hemolysis associated with QS-21, but not **TQL-1055**

- Weight loss associated with QS-21 containing vaccine, but not vaccine containing **TQL-1055**



Background: QS-21 Tolerability

- QS-21 administered subcutaneously to patients with malignant melanoma
- Doses from 10 to 200 mcg
- Local and systemic reactions showed a dose-dependent increase in frequency and severity (table, right)
  - **Mild** reactions at 10 and 50 mcg
  - **Moderate** and prolonged local reactions at 100 mcg
  - **Severe** local reactions and increased systemic reactions at 200 mcg
- Cf. QS-21 dose of 50 mcg (liposomal) in Shingrix

Table 1 Number of adverse reactions occurring (and their severity) at each QS-21 dose in patients receiving vaccines containing 500 μg GM2–KLH ± QS-21

	Dose of QS-21 (μg) (no. of vaccinations)				
Adverse reactions	0 (35)	10 (22)	50 (34)	100 (44)	200 (23)
Local					
Tenderness and pain	6 (1)	7 (1)[a]	21 (1)	34 (2)	23 (2)
Erythema and induration	6 (1)	4 (1)	17 (1)	24 (2)	21 (3)
Systemic					
Fever	0	0	3 (1)	2 (1)	7 (1)
Headache	0	0	0	0	1 (1)
Myalgia	0	1 (1)	2 (1)	0	6 (1)
Nausea or vomiting	0	1 (1)	1 (1)	0	1 (1)

Source: Livingston Vaccine 1994
Severity graded according to NCI CTC guidance
Median severity in parentheses: (1) mild (2) moderate (3) severe

Pertussis Acellular Vaccine Adjuvanted (PAVA) Phase 1 Interim Data

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PAVA Phase 1: Study Design

Healthy adults 18 to 50, >3 yrs post pertussis booster

N = 72, 12 per group randomized 10:2

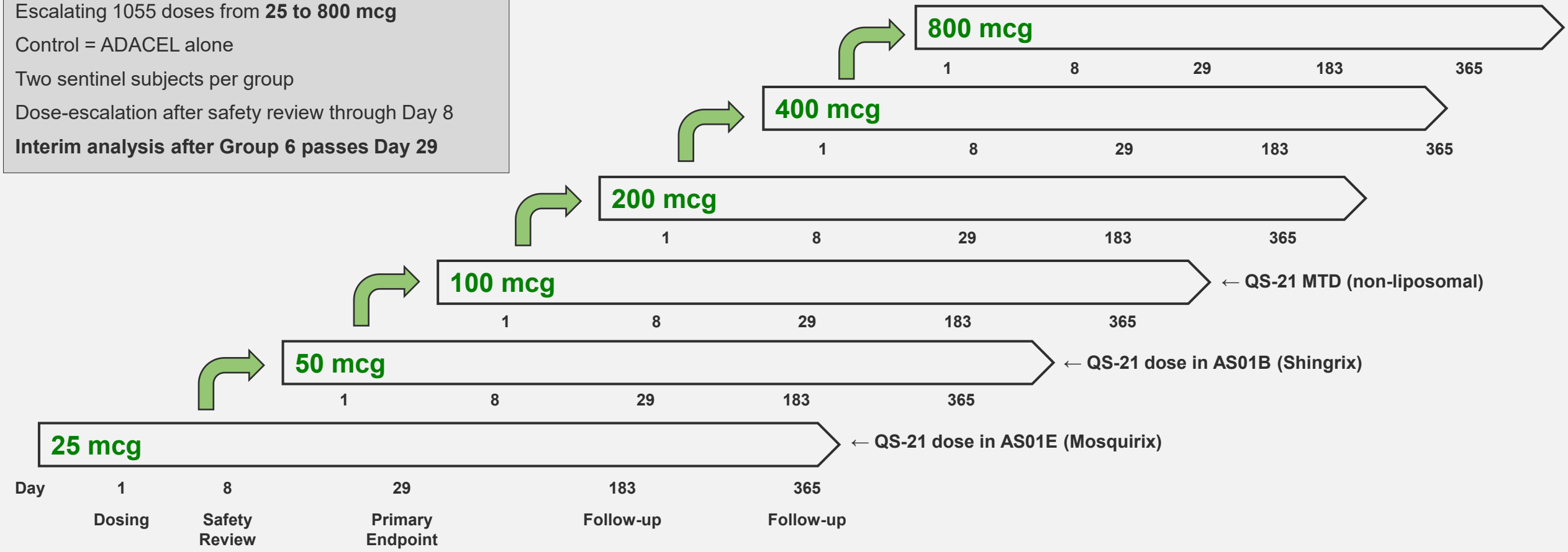
Escalating 1055 doses from **25 to 800 mcg**

Control = ADACEL alone

Two sentinel subjects per group

Dose-escalation after safety review through Day 8

Interim analysis after Group 6 passes Day 29



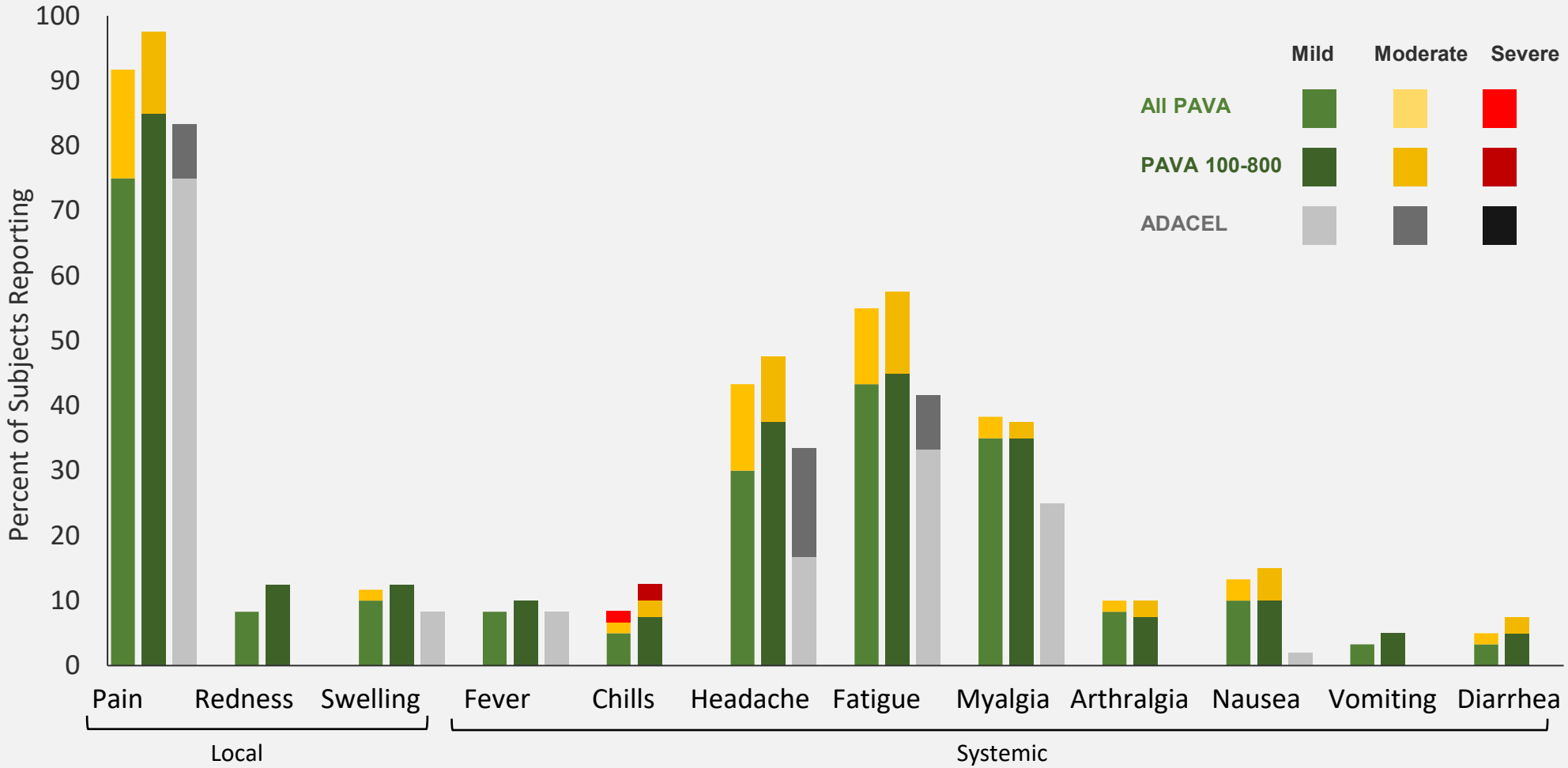
PAVA Phase 1: Demographics

Treatment Group	PAVA 25	PAVA 50	PAVA 100	PAVA 200	PAVA 400	PAVA 800	All PAVA	ADACEL Control
n	10	10	10	10	10	10	60	12
Age, years								
Median	32	26	28	39	26	28	**28**	**27**
Range	22-50	21-50	18-49	19-46	19-44	19-47	**18-50**	**20-47**
Race, n (%)								
White	6 (60)	9 (90)	9 (90)	8 (80)	9 (90)	8 (80)	**49 (82)**	**10 (83)**
Asian	3 (30)	1 (10)	0	1 (10)	0	1 (10)	**6 (10)**	**2 (17)**
Pacific Islander	1 (10)	0	1 (10)	0	1 (10)	0	**3 (5)**	**0**
Other	0	0	0	0	0	0	**0**	**0**
Sex, n (%)								
Female	3 (30)	4 (40)	6 (60)	7 (70)	4 (40)	6 (60)	**30 (50)**	**7 (58)**
Male	7 (70)	6 (60)	4 (40)	3 (30)	6 (60)	4 (40)	**30 (50)**	**5 (42)**
BMI, kg/m^2								
Median	22.3	26.3	24.4	24.6	28.1	25.1	**24.9**	**26.8**

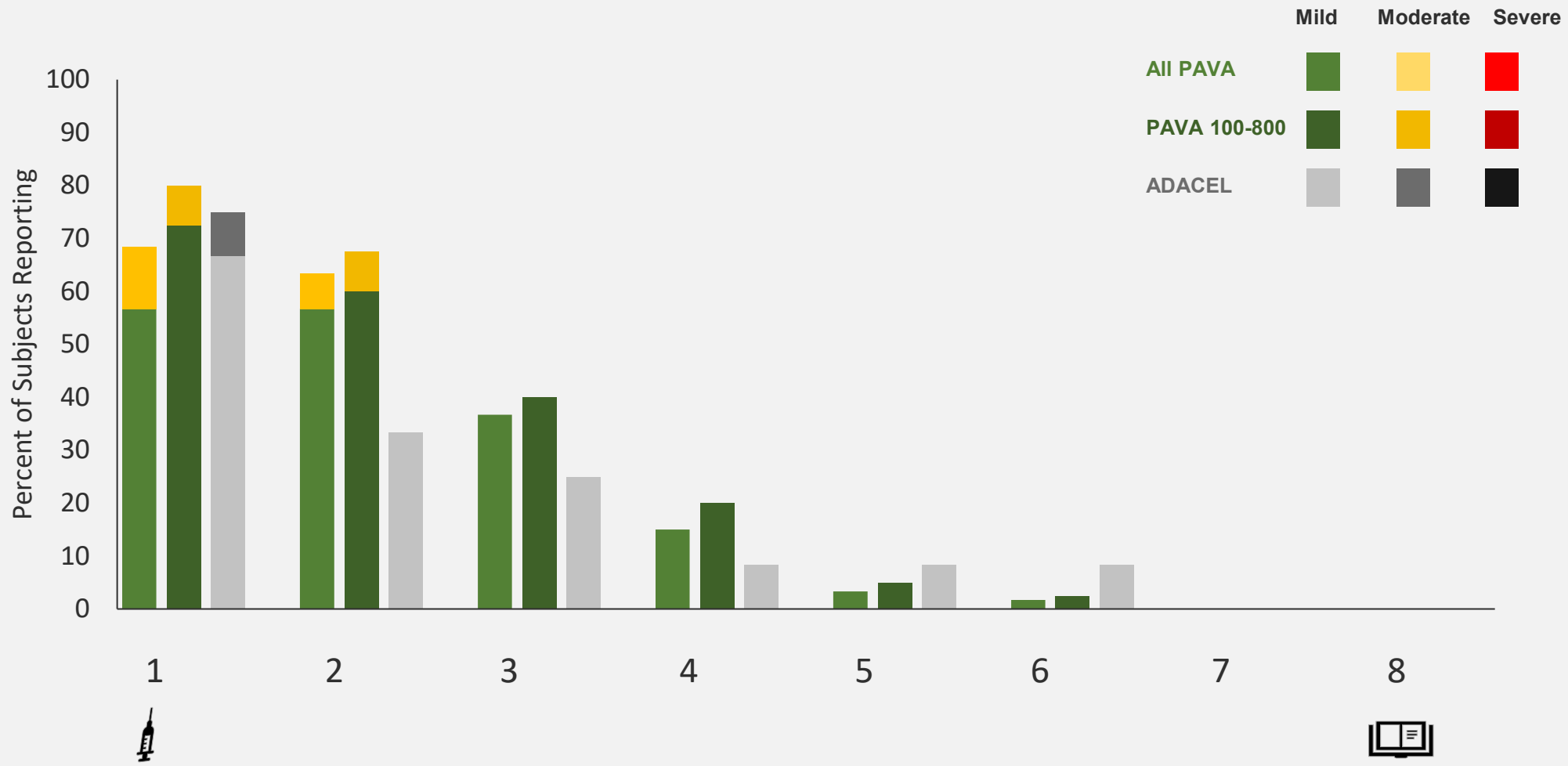
PAVA Phase 1: Overview of Safety

Treatment Group	PAVA 25	PAVA 50	PAVA 100	PAVA 200	PAVA 400	PAVA 800	All PAVA	PAVA 100-800	ADACEL Control
N	10	10	10	10	10	10	60	40	12
Solicited AEs, n (%)									
Any Local	**6 (60)**	**7 (70)**	**9 (90)**	**10 (100)**	**6 (60)**	**9 (90)**	**47 (78)**	**34 (85)**	**9 (75)**
Local Severe	0	0	0	0	0	0	0	0	0
Any Systemic	**8 (80)**	**7 (70)**	**8 (80)**	**6 (60)**	**7 (70)**	**7 (70)**	**43 (72)**	**28 (70)**	**7 (58)**
Systemic Severe	0	0	0	0	1 (10)	0	1 (2)	1 (3)	0
Unsolicited AEs, n (%)									
Any	4 (40)	0	2 (20)	4 (40)	3 (30)	2 (20)	15 (25)	11 (28)	4 (33)
Related	1 (10)	0	0	1 (10)	1 (10)	0	3 (5)	2 (5)	2 (17)
MAAE	0	0	0	0	2 (20)	1 (10)	3 (5)	3 (8)	0
PIMD	0	0	0	0	0	0	0	0	0
SAE	0	0	0	0	0	0	0	0	0
Pregnancy	0	0	0	0	0	0	0	0	0
Death	0	0	0	0	0	0	0	0	0

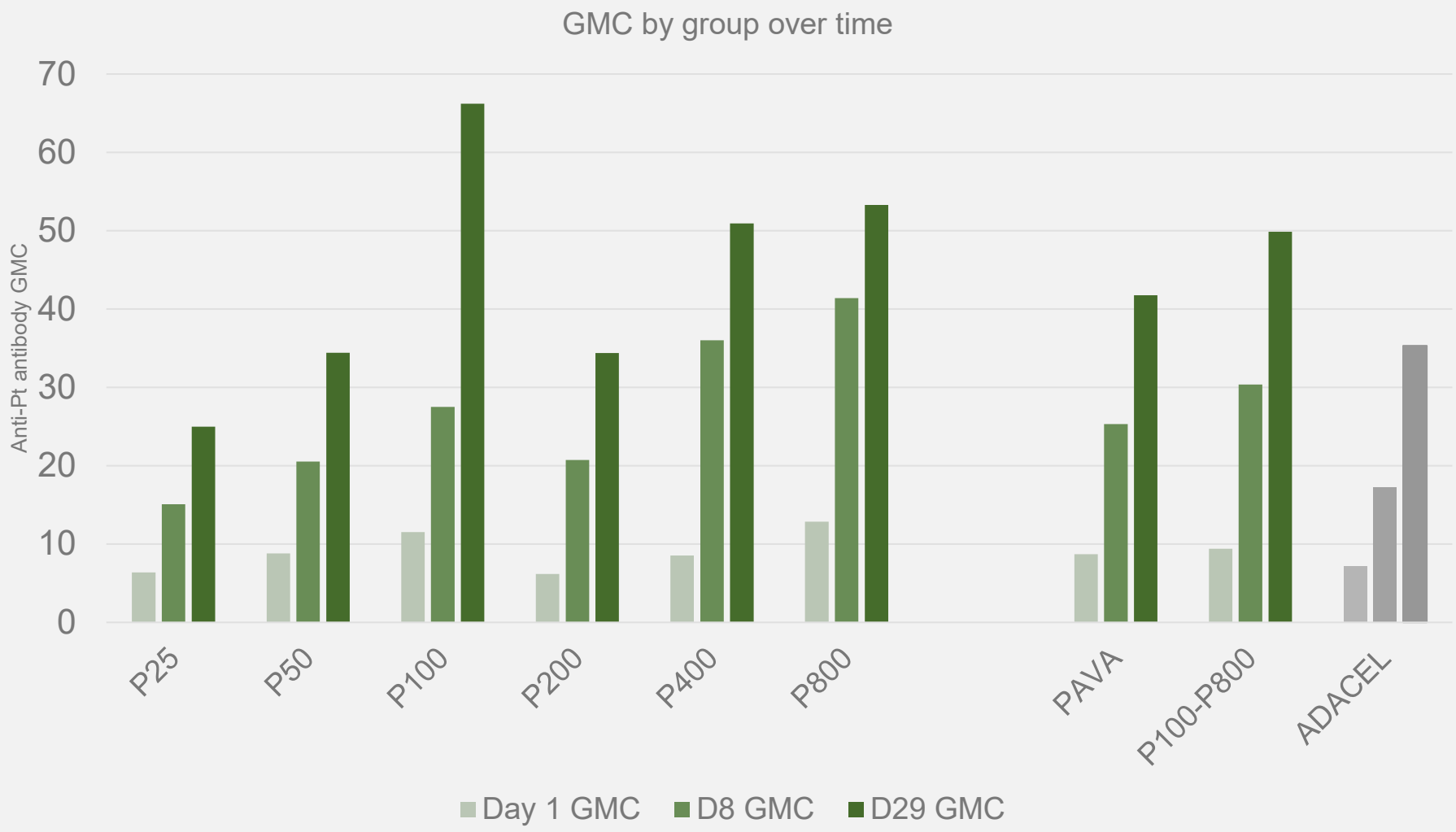
PAVA Phase 1: Post-Injection Reactions by Event



PAVA Phase 1: Injection Site Pain by Day



PAVA Phase 1: Anti-PT Antibodies (GMC)

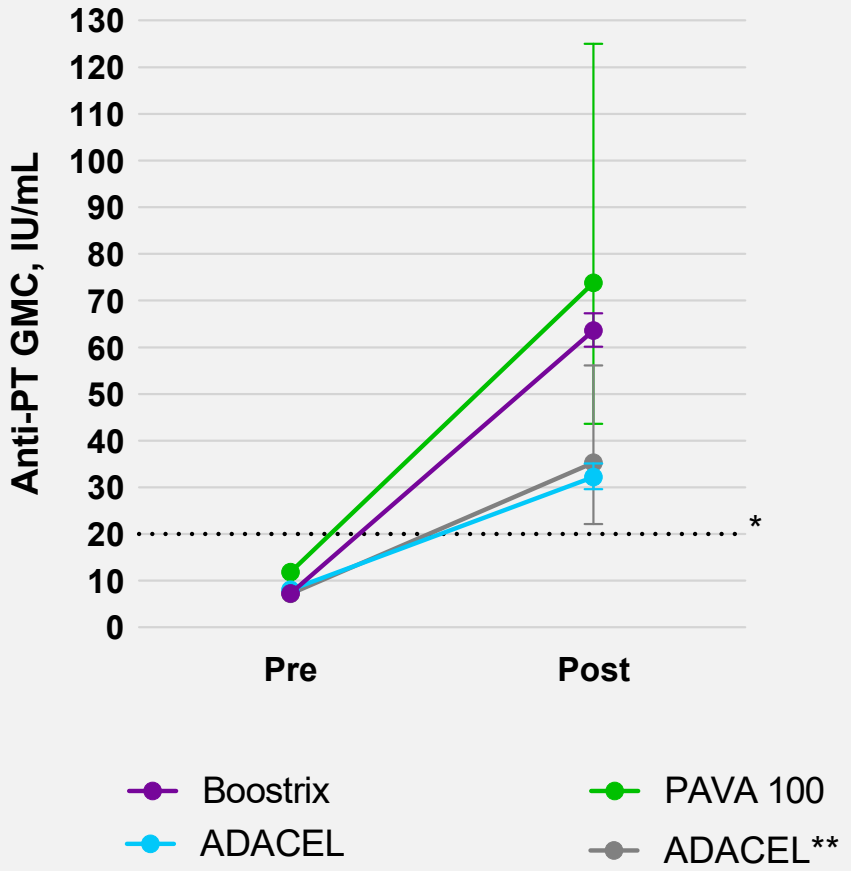


PAVA Phase 1: Cross-Study Comparison of GMC

Treatment Group		Boostrix (Brandon 2018)	ADACEL (Brandon 2018)	PAVA 100µg (PAVA Ph 1)	ADACEL (PAVA Ph 1)
n		1448	728	40	12
28d Post	**GMC**	**63.6**	**32.2**	**66.2**	**35.3**
	95% CI	60.1 - 67.3	29.6 - 35.1	39.2-111.7	22.2 - 56.2

PAVA Phase 1 Interim Data: Summary and Conclusions

- PAVA was well tolerated at doses up to 800 mcg
- PAVA's safety profile was similar to ADACEL's
- Local and systemic reactions were predominantly mild
- An anti-PT response was observed in all groups
- The 100, 400, and 800 mcg dose groups individually showed a trend toward higher GMC
- The 100-800 mcg groups (pooled) had a significantly higher Day 29 anti-PT GMC than ADACEL**
- Further interpretation of immunogenicity was limited by sample size



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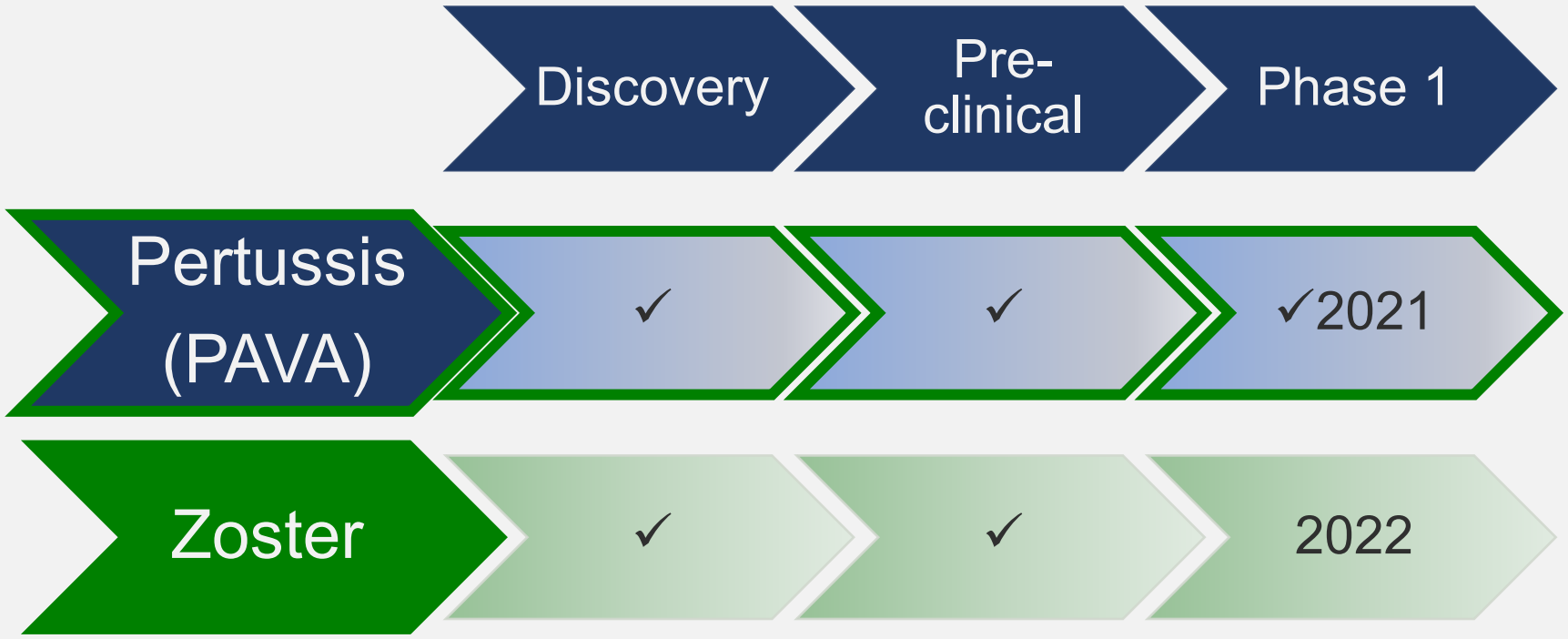
PAVA Phase 1: Next Steps

- Analysis of additional antibodies pending
  - Additional antibodies (Pertactin, Fimbriae 2/3, Diphtheria) expected
- Long-term follow-up ongoing
  - Day 182 complete Jan 2022
  - Day 365 (end of study) complete July 2022

Pipeline of vaccine candidates



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Improved herpes zoster vaccine

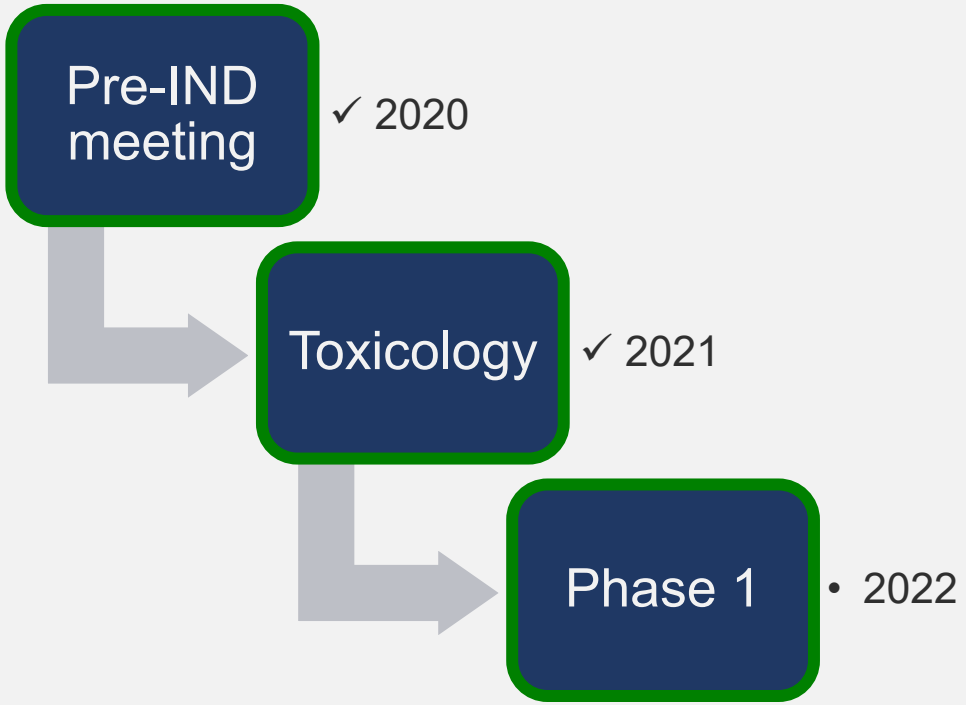
Our promise:

Better tolerated herpes zoster vaccine

Adverse Event (AE)	Placebo	Shingrix®
Any solicited AE	34% (32-35)	84% (83-86)
Solicited **local** AE	12% (11-13)	81% (80-82)

Our progress:

Phase 1 planned for 2022



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Thank you!

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