A Randomized Placebo-Controlled Trial of a Conjugate Nicotine Vaccine (NicVAX®) in Smokers Who Want to Quit: 12 Month Results

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Presenter Disclosure Information

Stephen I Rennard
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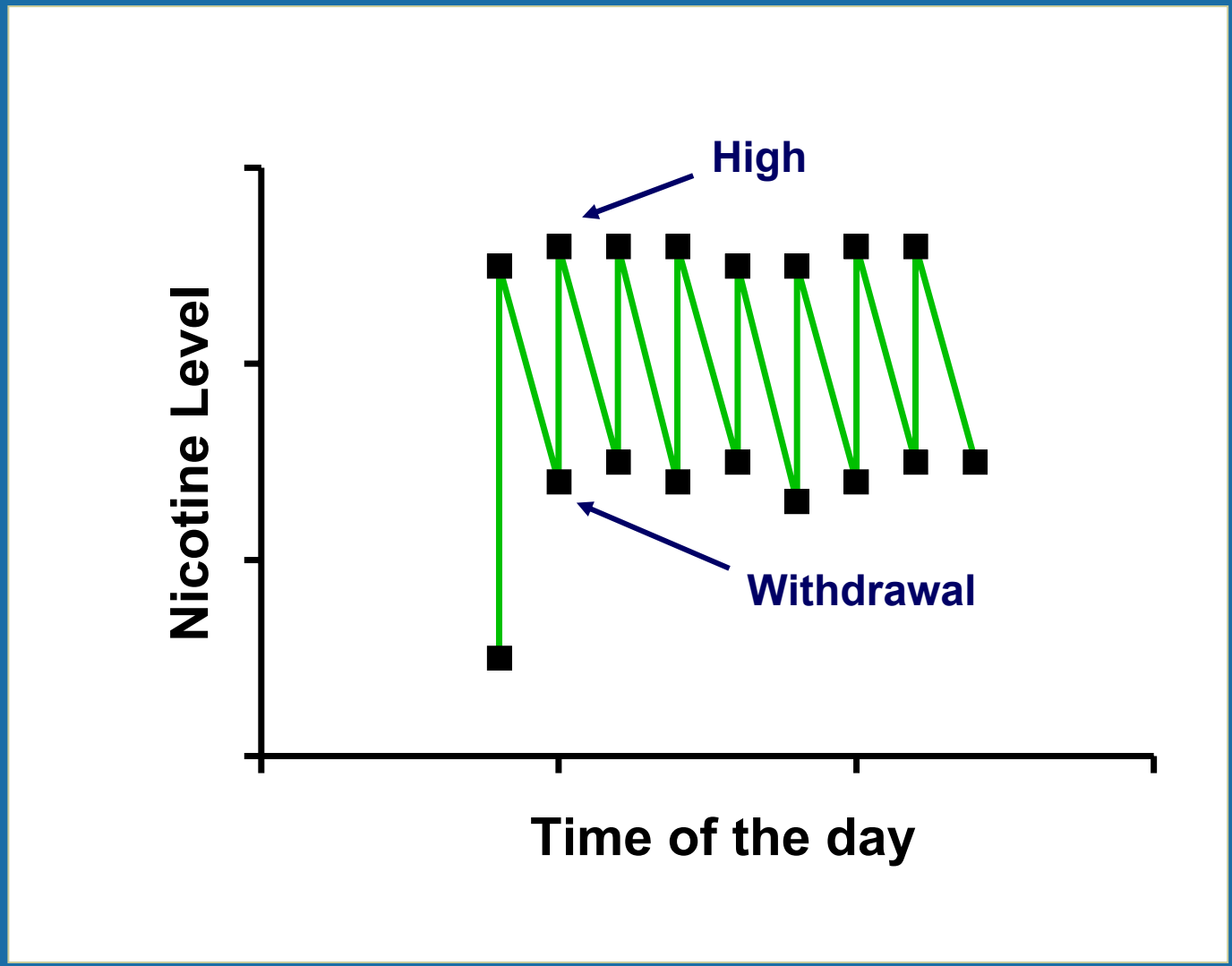
NicVAX® is investigational

DISCLOSURE INFORMATION:
The following relationships exist related to this presentation:

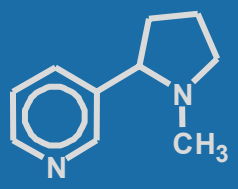
University of Nebraska Medical Center (S. Rennard, PI) received a research contract from Nabi to conduct this and one other clinical trial

Since 2006, Dr. Rennard has conducted clinical trials or consulted with the following companies on the topic of smoking cessation: Pfizer, Novartis, GSK

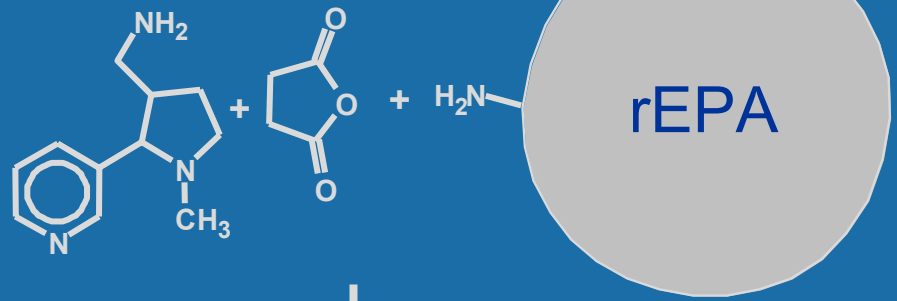
Nicotine Levels in a Smoker



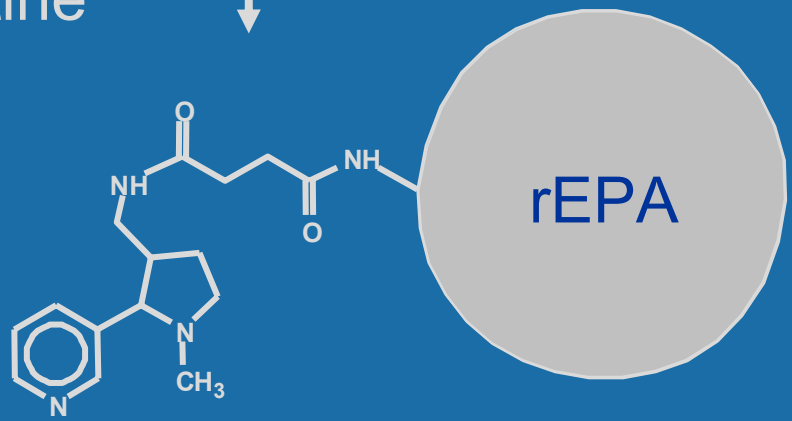
3'aminomethyl Nicotine – Recombinant Ps. aeruginosa Exoprotein A (rEPA) Conjugate

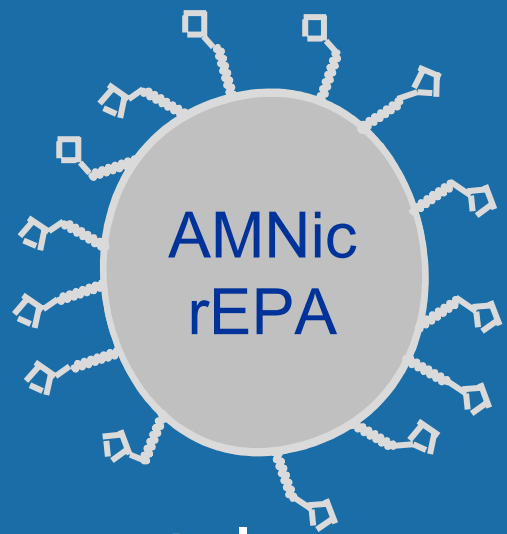


Nicotine



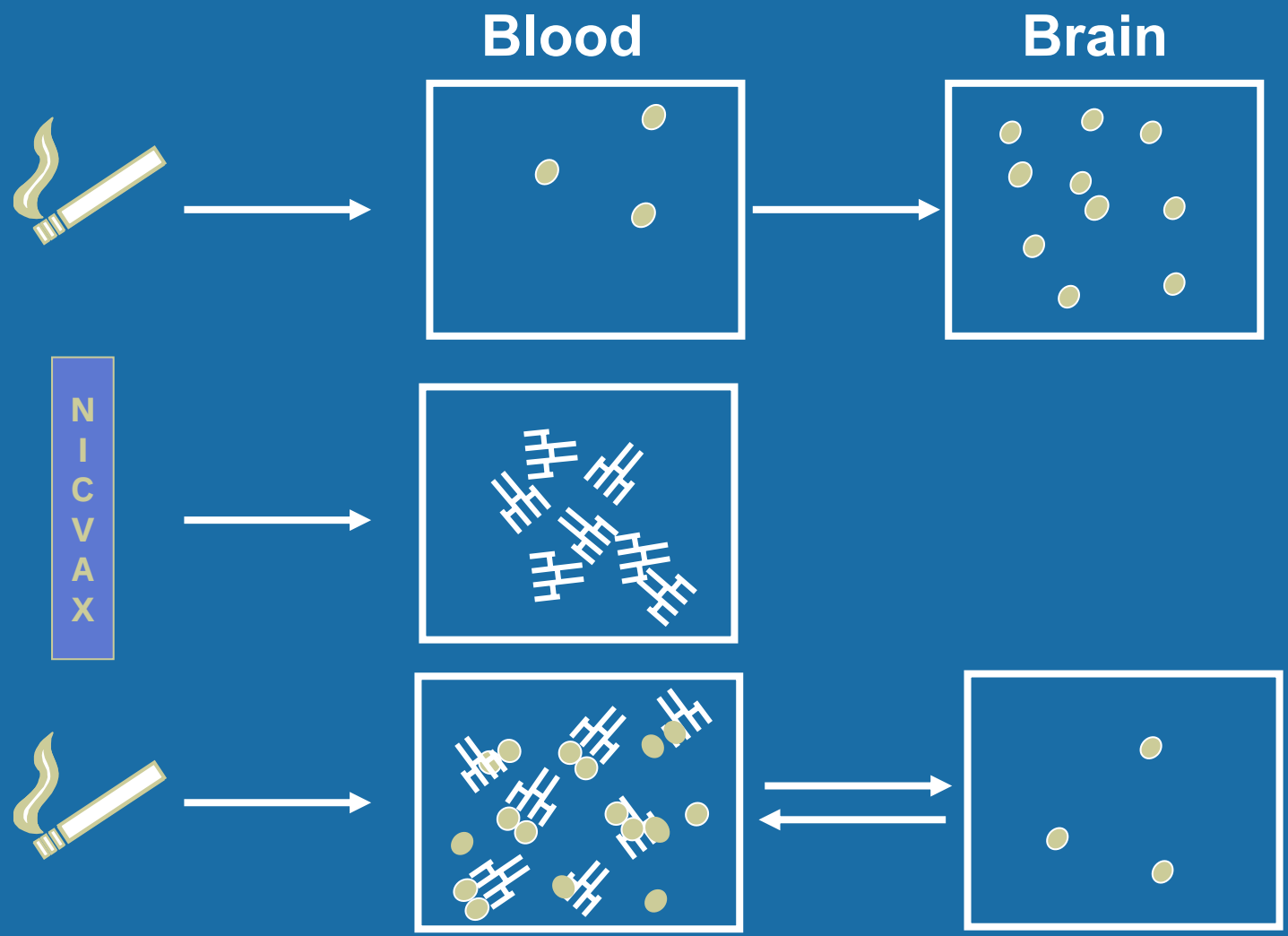
3' aminomethyl Nicotine





+ alum
(Adjuant)

AMNic-rEPA (NicVAX) Antibodies Function: Capture Release Mechanism

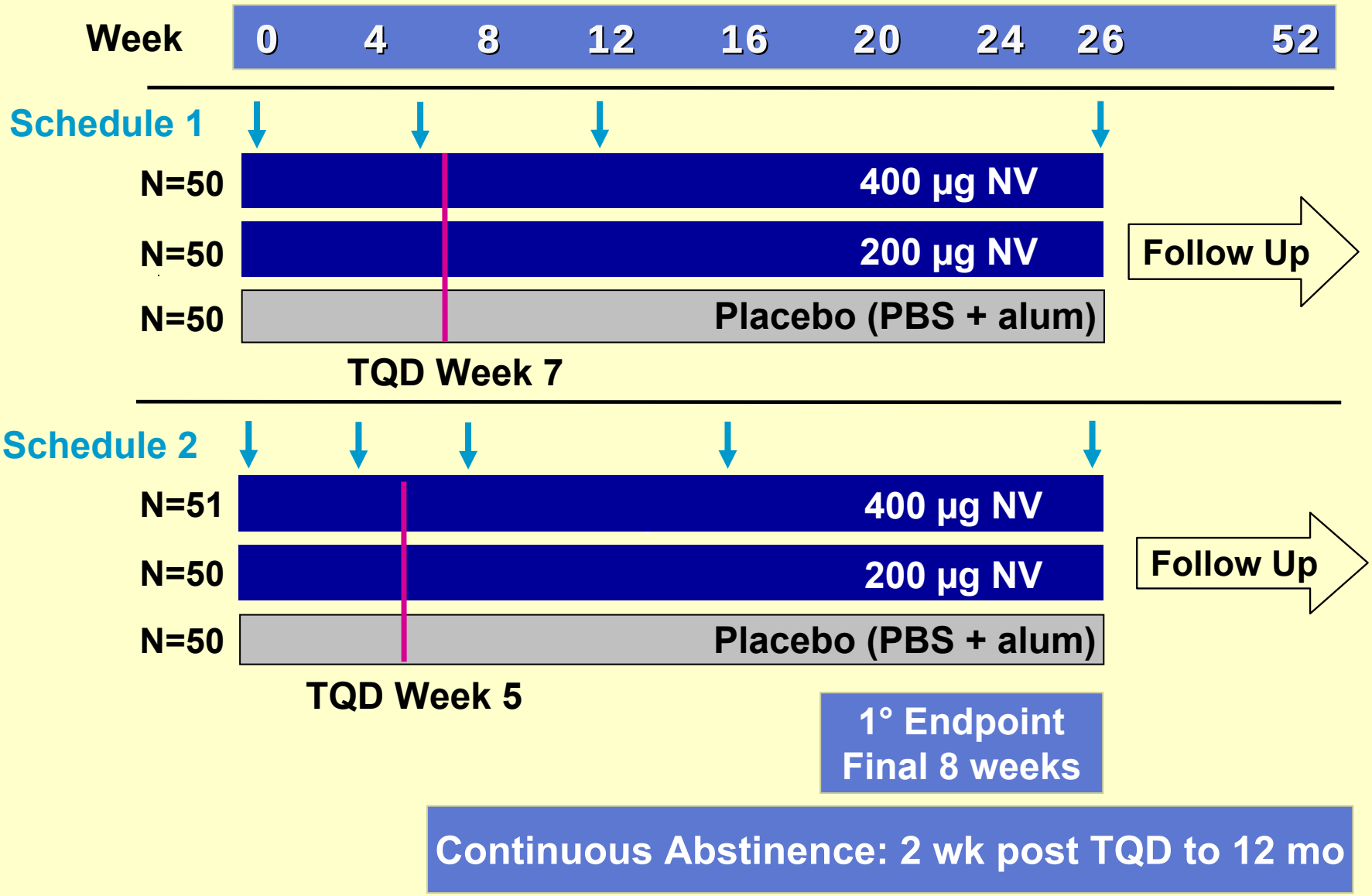


Phase 2 Study: Key Questions

- **Determine most effective dose and immunization schedule**
- **Determine if vaccination is associated with long term quits**
- **Determine if antibody response is associated with long term quits**

NicVAX Phase IIb Trial Design

A randomized, double-blind, placebo-controlled trial



Study Population

Demographics		NicVax n=201	Placebo n=100
Gender	Males	54%	50%
	Females	46%	50%
Age	Mean Age	48	47
Ethnicity	Not Hispanic	98%	98%
Race	Asian	1%	3%
	Black	5%	7%
	Islander	1%	0%
	White	91%	88%
	Other	2%	2%

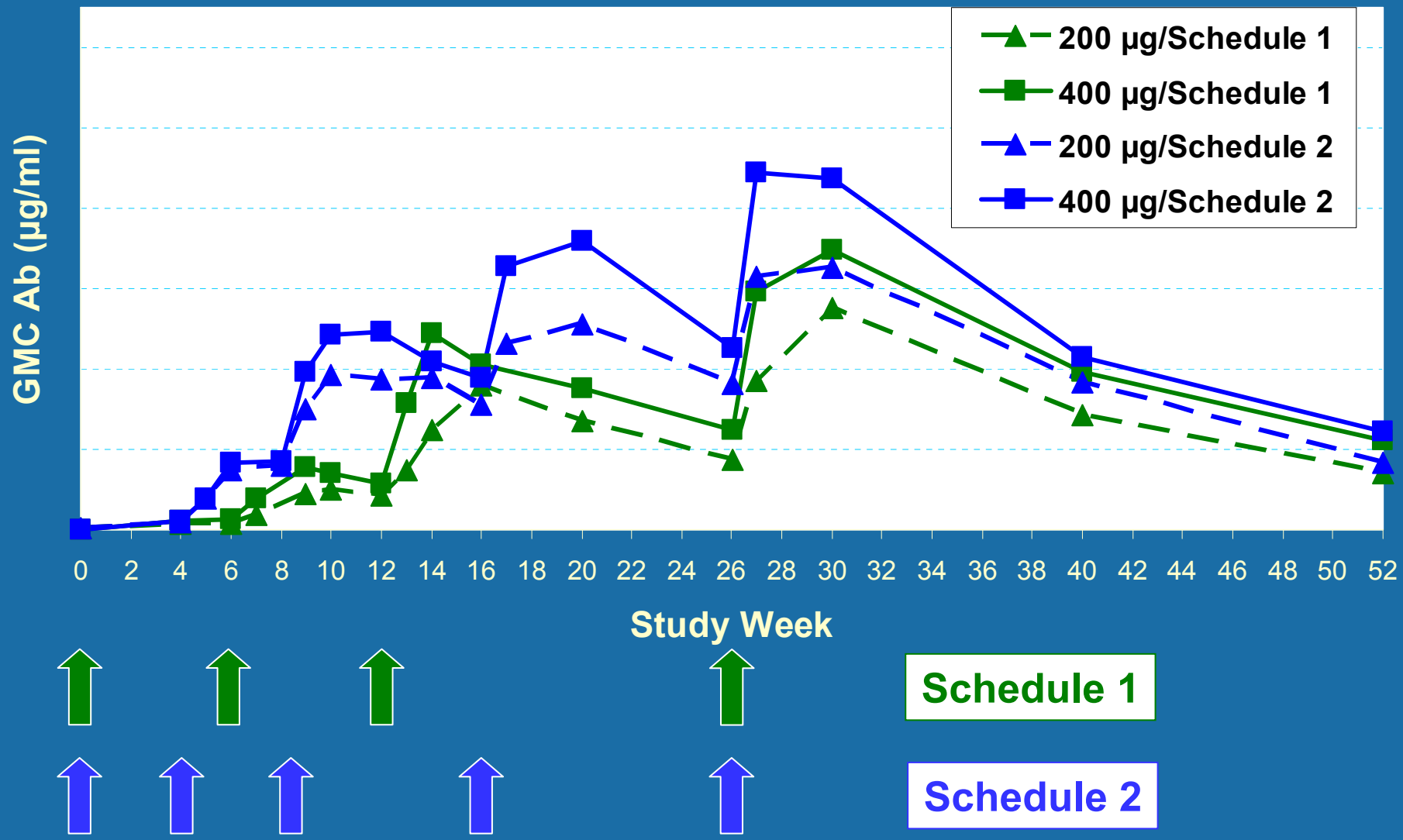
Baseline Smoking Characteristics	NicVAX N=201	Placebo n=100
Mean Number Cigarettes Smoked Per Day	24.3	24.8
Mean FTND Score	6.12	6.05
Subjects with at least 1 previous quit attempt	96%	96%

*Early Terminated Subjects**

		Schedule 1		Schedule 2	
	Placebo	200 µg	400 µg	200 µg	400 µg
All Subjects	100	50	50	50	51
Early Terminated Total	33 (33%)	16 (32%)	12 (24%)	24 (48%)	22 (43%)
Lost to Follow-Up	6 (6%)	5 (10%)	4 (8%)	5 (10%)	6 (12%)
Non-Compliant with Protocol	1 (1%)	0	0	1 (2%)	2 (4%)
Protocol Violation	0	0	0	0	2 (4%)
Withdrawal of Consent	23 (23%)	11 (22%)	7 (14%)	16 (32%)	7 (14%)
Adverse Event	2 (2%)	0	1 (2%)	2 (4%)	4 (8%)
Other	1 (1%)	0	0	0	1 (2%)

*All Early Terminations are coded as smoking thereafter.

Antibody Concentration Over Time
Schedule 1 & Schedule 2



12-Month Continuous Abstinence

Intent to Treat Population

	Schedule 1	Schedule 2
NicVAX *400 µg*	6% (n=3/50) p=0.96	16% (n=8/51) p=0.038
NicVAX *200 µg*	6% (n=3/50) p=0.88	14% (n=7/50) p=0.056
Placebo	6% (n=6/100)	

Continuous Abstinence at 12 Months by Anti-Nicotine Antibody Levels

	12-Month Abstinence
NicVAX *High Antibody**	16% (n=10/61) p=0.03
NicVAX *Low Antibody*	8% (n=11/140) p=0.49
Placebo	6% (n=6/100)

***Top 30% by AUC per protocol**

Continuous Abstinence at 12 Months by Anti-Nicotine Antibody Levels, Dose & Schedule

12-Month Continuous Abstinence Rates (44 wks)	Schedule 2		Schedule 1	
	400 µg	200 µg	400 µg	200 µg
NicVAX *High Antibody**	21% (n=4/19) p=0.038	19% (n=3/16) p=0.056	13% (n=2/16) p=0.57	10% (n=1/10) p=0.84
NicVAX *Low Antibody*	13% (n=4/32) p=0.22	12% (n=4/34) p=0.23	3% (n=1/34) p=0.36	5% (n=2/40) p=0.55
Placebo	6% (n=6/100)			

*Top 30% by AUC per protocol

Antibody-Dependent Reduction in Cigarette Consumption in Non-Quitters

	Average Daily Cigarette Consumption (median, inter-quartile range)			
	Baseline	6-Months	12-Months	% Baseline @ 12-months
NicVAX *High Antibody**	20 18-25	7.5 4-16	10 4-19	50%
NicVAX *Low Antibody*	20 20-30	13 6-18.5	16 5-20	80%
Placebo	20 20-30	13 5-19	14 7-20	70%

*Top 30% by AUC per protocol

Adverse Events

	NicVAX n=201	Placebo n=100
Upper Respiratory Infection	29%	30%
Headache	12%	12%
Insomnia	10%	9%
Nasopharyngitis	9%	14%
Nausea	7%	10%
Dizziness	6%	11%

All events ≥ 10% of either NicVAX or Placebo

Adverse events leading to early terminations

- **Nicvax groups (7/201):**
  - Anaphylactic reaction
  - Increasing frequency of migraine headaches
  - Arthralgias in multiple joints
  - Shingles
  - Stiffness in left hand
  - Dozing off at the wheel
  - Atrial fibrillation

- **Placebo (2/100):**
  - Forgetfulness
  - Exacerbation of Crohn's disease

Local Reactogenicity – Percentage of Subjects Experiencing Events (ITT)

Injection	1		2		3		4		5	
	NV†	Pbo‡	NV	Pbo	NV	Pbo	NV	Pbo	NV	Pbo
Ache	75	83	84	85	73	81	77	69	79	68
Burning	19	17	21	24	24	19	28	13	28	6
Heat	17	18	28	30	32	21	32	20	29	15
Swelling	32	41	45	38	46	31	43	25	38	27
Redness	14	18	26	18	34	19	28	11	24	9
Tenderness	78	91	87	89	81	81	80	77	83	77

† NV = NicVAX ‡ Pbo = Placebo

Systemic Reactogenicity – Percentage of Subjects Experiencing Events (ITT)

Injection	1		2		3		4		5	
	NV†	Pbo‡	NV	Pbo	NV	Pbo	NV	Pbo	NV	Pbo
Fever	2	2	3	2	8	7	6	3	0	0
General Dis-comfort / Malaise	50	58	64	52	50	49	46	41	36	32
Headache	41	41	54	36	44	35	34	27	33	21
Muscle Aches / Myalgia	65	64	66	64	55	62	57	57	50	59
Nausea	18	22	28	21	18	13	12	12	19	15
Vomiting	1	2	5	2	1	0	4	5	4	3

† NV = NicVAX ‡ Pbo = Placebo

Conclusions

- **Most effective dose and schedule identified: Schedule 2 (5 injections), 400 µg**
- **Antibody level predicts continuous abstinence**
- **Significantly increased abstinence through 12 months**
- **Safety profile**
  - Reactogenicity and adverse events similar to placebo
  - No evidence of compensatory smoking or increase in withdrawal symptoms

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