AAIC Panel
July 28, 2021

Symbol: **ANVS** (NYSE American)

NEUROTOXIC PROTEINS IMPAIR AXONAL TRANSPORT AND **CAUSE A TOXIC CASCADE**

HIGH LEVELS OF NEUROTOXIC PROTEINS

- IMPAIRED AXONAL TRANSPORT
- SLOWER SYNAPTIC TRANSMISSION
- INFLAMMATION
- DEATH OF NERVE CELLS
- LOSS OF COGNITIVE AND MOTOR FUNCTION

Posiphen LOWERS LEVELS OF NEUROTOXIC PROTEINS

- IMPROVED AXONAL TRANSPORT
- INCREASED SYNAPTIC TRANSMISSION
- NO INFLAMMATION
- HEALTHY NERVE CELLS
- IMPROVED COGNITIVE AND MOTOR FUNCTION

Posiphen IMPROVES AXONAL TRANSPORT AND **IMPEDES THE TOXIC CASCADE**

TWO PHASE 2 CLINICAL TRIALS

	AD Trial	PD Trial
Therapeutic Area	Early to Moderate AD	Early to Moderate PD
Patients	14	14 + 40
Phase	2	
Sites	12	
Country	United States	
Design	Double-Blind, Placebo-Controlled, Biomarker Study	
Endpoints	Reversal of Toxic Cascade	
Exploratory	Efficacy	

TIMELINE OF PHASE 2 CLINICAL TRIAL IN AD AND PD

Efficacy and biomarker data as of July 2021.
Additional markers in CSF and plasma are still being measured

A meeting with the FDA to discuss the data from the AD and the PD study as well as from the chronic toxicology in rats and dogs is projected for Fall of 2021

REVERSAL OF TOXIC CASCADE: EFFICACY

Data from first 14 AD and 14 PD patients

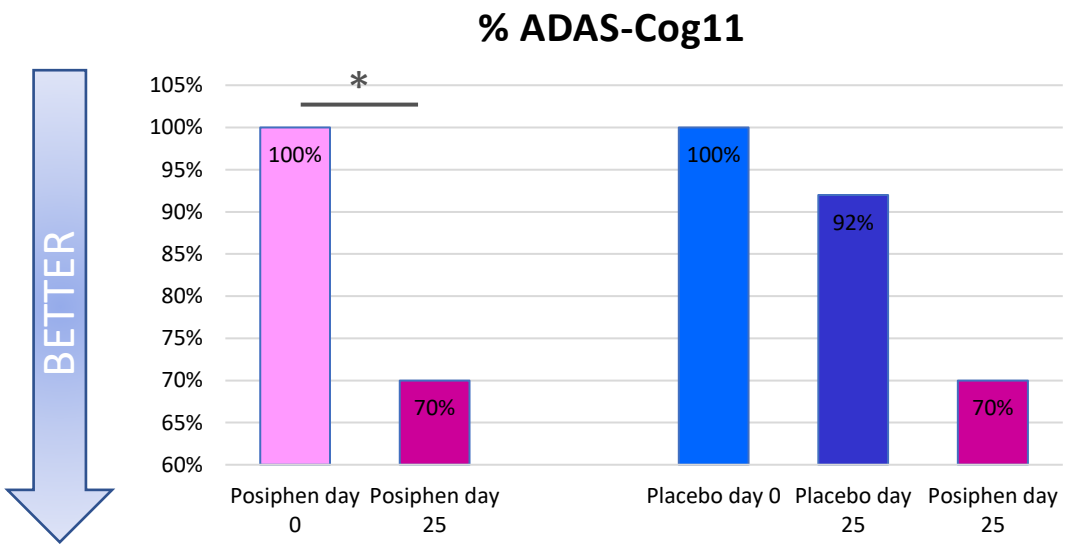
REVERSAL OF TOXIC CASCADE	EXPECTED OUTCOME	ACTUAL OUTCOME	
		AD	PD
Neurotoxic proteins	↓		
Axonal transport	↑		
Axonal damage	↓		
Inflammation	↓		
Synaptic Markers	↓		
Control proteins	0		
Efficacy: WAIS coding	↑	↑	↑
Efficacy: Motor function	↑		↑
Efficacy: Cognition	↑	↑	

BASELINE DEMOGRAPHICS

	ALZHEIMER			PARKINSON		
Patients Enrolled	Placebo (N=6)	Posiphen 80mg (N=10)	Total (N=16)	Placebo (N=5)	Posiphen 80mg (N=10)	Total (N=15)
Age (years)	68.0 (6.87)	72.8 (6.34)	71.0 (6.75)	75.4 (3.13)	65.0 (9.31)	68.5 (9.18)
Male	3 (50.0%)	2 (20.0%)	5 (31.3%)	3 (60.0%)	8 (80.0%)	11 (73.3%)
Female	3 (50.0%)	8 (80.0%)	11 (68.8%)	2 (40.0%)	2 (20.0%)	4 (26.7%)
HISPANIC	4 (66.7%)	5 (50.0%)	9 (56.3%)	2 (40.0%)	0 (0.0%)	2 (13.3%)
CAUCASIAN	2 (33.3%)	5 (50.0%)	7 (43.8%)	3 (60.0%)	10 (100.0%)	13 (86.7%)
WHITE	4 (66.7%)	8 (80.0%)	12 (75.0%)	5 (100.0%)	10 (100.0%)	15 (100.0%)
AFRICAN AMERICAN	1 (16.7%)	0 (0.0%)	1 (6.3%)	0	0	0
ASIAN	1 (16.7%)	1 (10.0%)	2 (12.5%)	0	0	0
NATIVE HAWAIIAN	0 (0.0%)	1 (10.0%)	1 (6.3%)	0	0	0

EFFICACY IN AD PATIENTS – ADAS-Cog11

Data from 14 AD patients

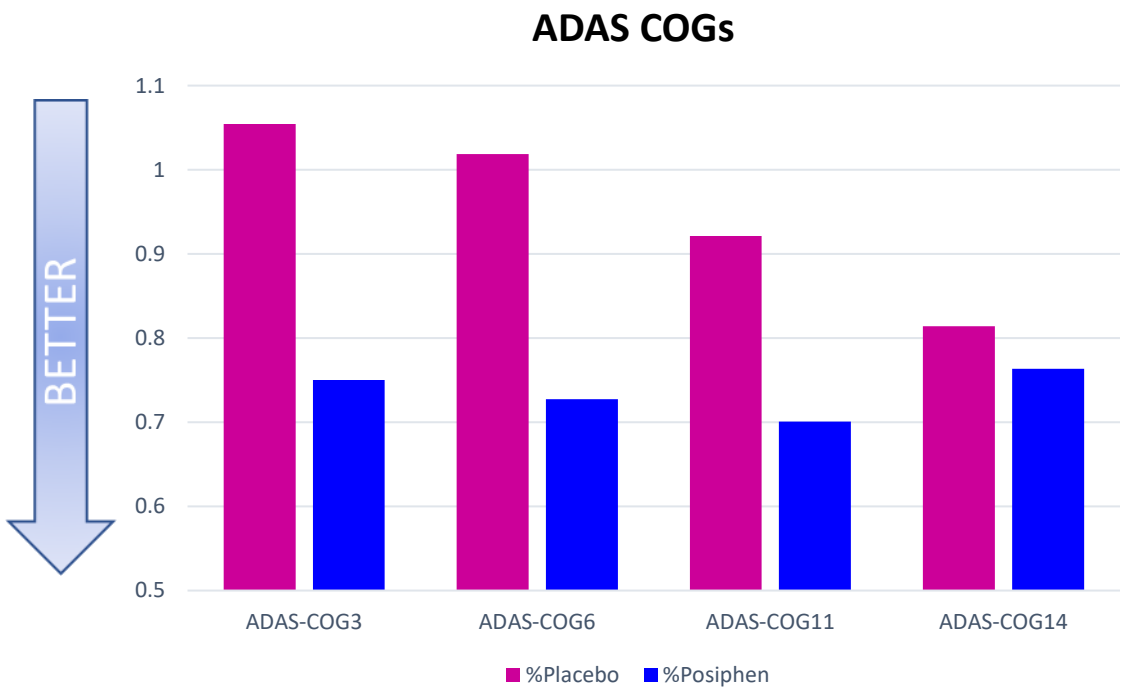


Left: From baseline to 25 days in the Posiphen-treated group, ADAS-Cog11 improved by 4.4 points, a statistically significant improvement of 30% ($p<0.05$).

Right: Posiphen-treated group compared to placebo group at baseline and 25 days showed an improvement of 3.3 points, or 22% ($p= 0.13$).

EFFICACY IN AD PATIENTS – ADAS-Cogs11

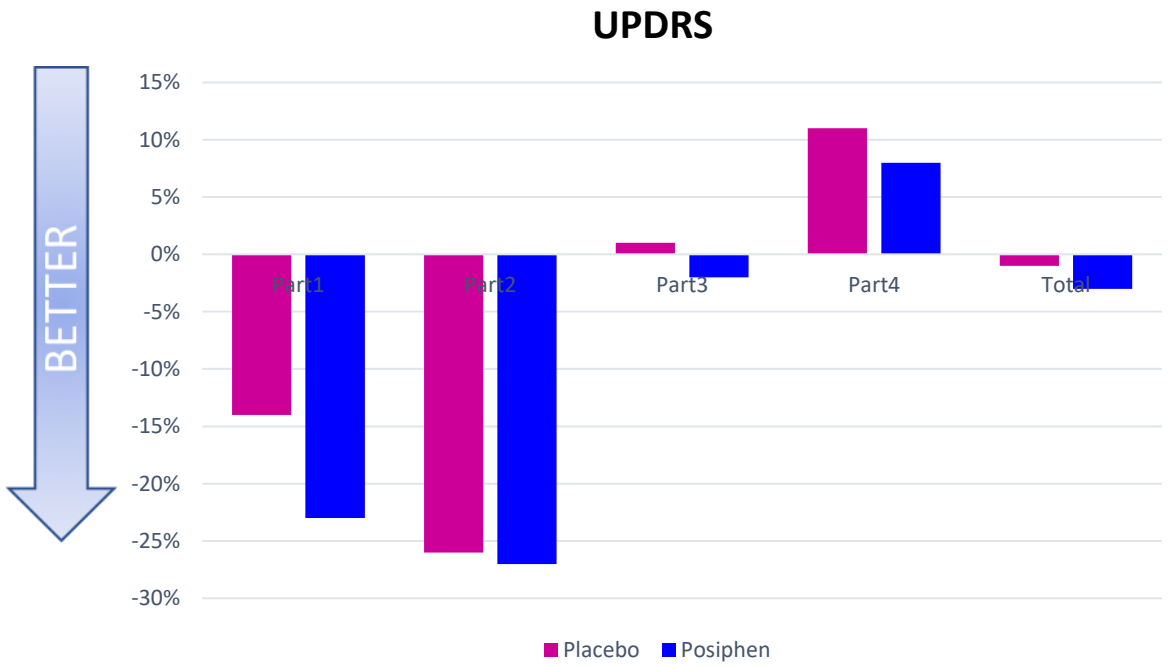
Data from 14 AD patients



Posiphen-treated group showed trends of improvement in all four ADAS-Cog tests performed compared to placebo group.

EFFICACY IN PD PATIENTS – MDS-UPDRS TEST

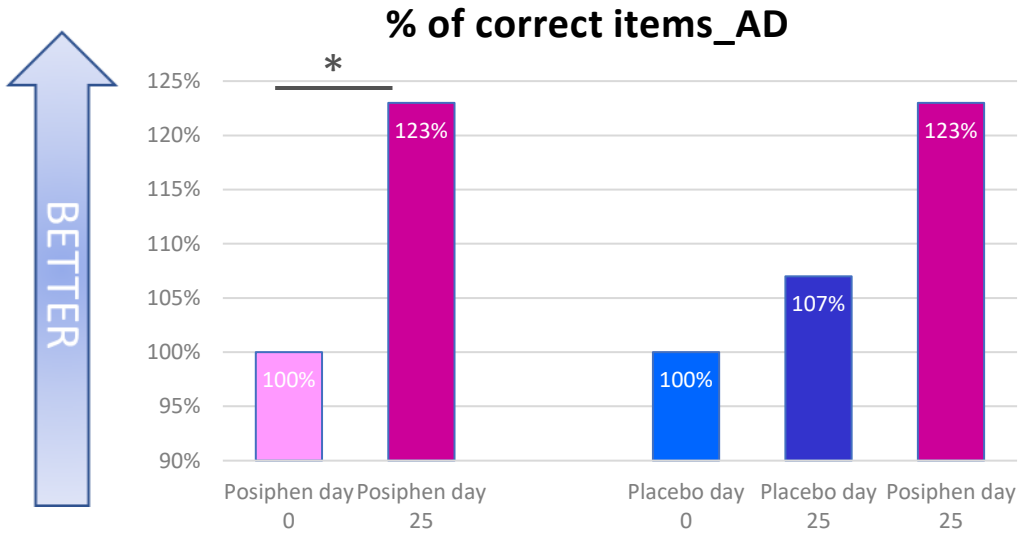
Data from 14 PD patients

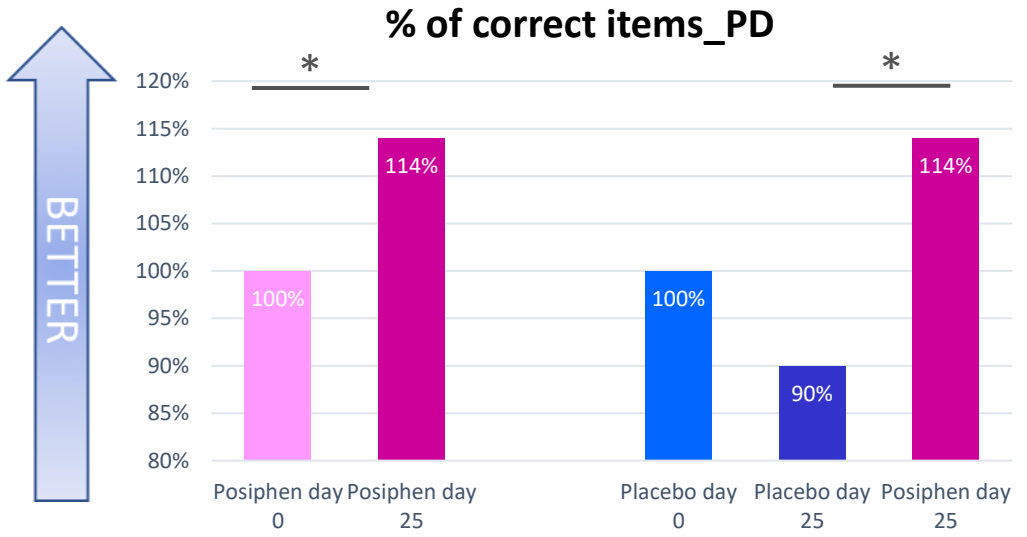


Posiphen-treated group showed trends of improvement in all four parts of UPDRS test compared to placebo group.

EFFICACY IN AD AND PD PATIENTS – WAIS CODING TEST

Data from 14 AD and 14 PD patients





The WAIS coding test measures speed in movement and thinking. Treated AD patients show a 6.6 point and PD patients a 6.1-point improvement in coding after Posiphen treatment.

This is the first double-blind, placebo-controlled study that shows cognitive improvements in AD patients as measured by ADAS-Cog and functional improvements in PD patients as measured by the Unified Parkinson's Disease Rating Scale (UPDRS).

EFFICACY IN AD AND PD PATIENTS - MMSE

MMSE	AD		PD	
	Placebo	Posiphen	Placebo	Posiphen
MMSE Baseline	24.5	25.4	27.6	29.1
25 Days later	25.7	26.2	28.0	29.1
Improvement in MMSE	1.2	0.8	0.4	0.0

While there is a positive trend in AD, the changes in MMSE are not statistically significant.

EFFICACY IN AD PATIENTS – CDR –SUM OF BOXES

CDR	Placebo	Posiphen
Improvement in total score	-1.17	-0.96

In AD patients there are positive trends in orientation, judgement and problem solving, home and hobbies as well as total CDR score, but the data is not statistically significant.

SAFETY SUMMARY

Data from first 14 AD and PD patients

	AD Patients			PD Patients		
	Placebo (N=6)	Posiphen 80mg (N=10)	Total (N=16)	Placebo (N=5)	Posiphen 80mg (N=10)	Total (N=15)
Subjects with any AEs	3 (50.0%)	5 (50.0%)	8 (50.0%)	3 (60.0%)	3 (30.0%)	6 (40.0%)
Number of AEs	4	7	11	5	3	8
Serious AEs	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
AEs that led to Drug Interrupted	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
AEs that led to Drug Withdrawn	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
AEs Suspected Drug Related	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)	0 (0.0%)	1 (6.7%)
AEs Study Procedure	3 (50.0%)	4 (40.0%)	7 (43.8%)	2 (40.0%)	1 (10.0%)	3 (20.0%)
CTCAE Grade 1	3 (50.0%)	4 (40.0%)	7 (43.8%)	3 (60.0%)	3 (30.0%)	6 (40.0%)
CTCAE Grade 2	0 (0.0%)	1 (10.0%)	1 (6.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Most AEs were due to the spinal fluid extraction that resulted in headaches and back aches

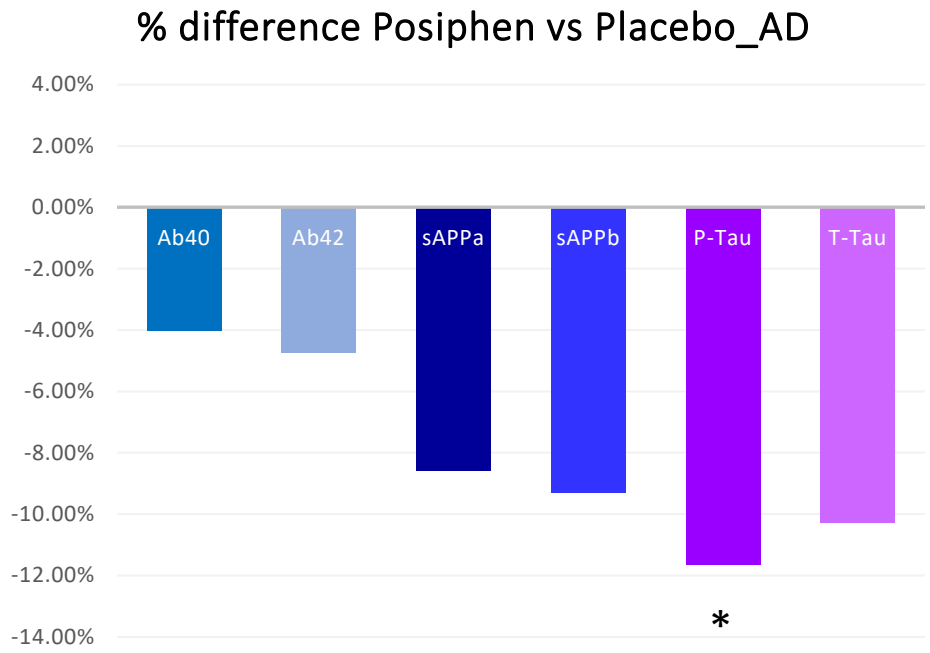
REVERSAL OF TOXIC CASCADE: MARKERS

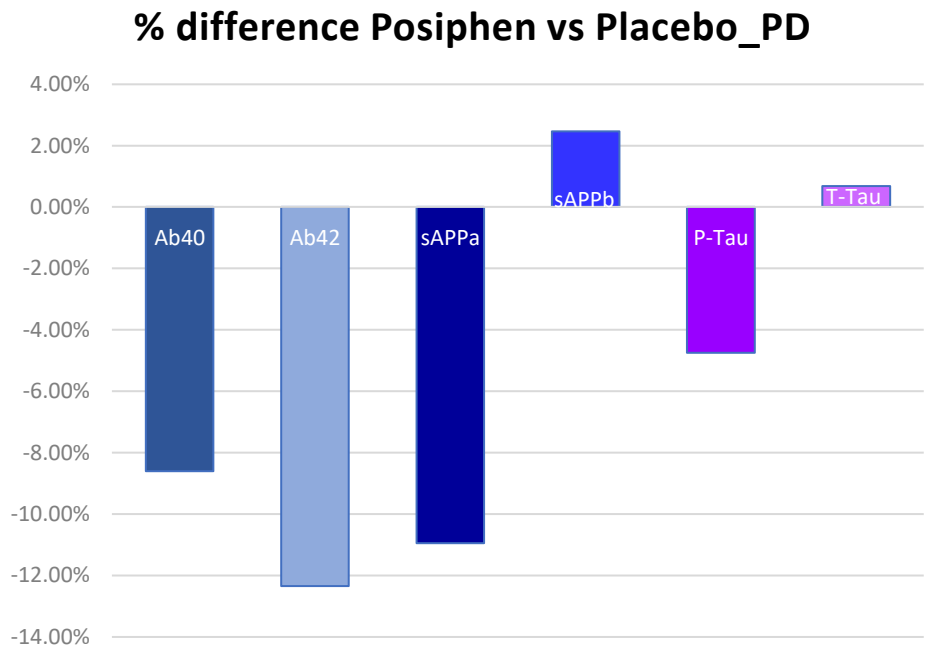
Data from first 14 AD and 14 PD patients

REVERSAL OF TOXIC CASCADE	EXPECTED OUTCOME	ACTUAL OUTCOME	
		AD	PD
Neurotoxic proteins	↓	↓	↓
Axonal transport	↑		
Axonal damage	↓	↓	↓
Inflammation	↓		↓
Synaptic Markers	↓		
Control proteins	0		
Efficacy: WAIS coding	↑	↑	↑
Efficacy: Motor function	↑		↑
Efficacy: Cognition	↑	↑	

STEP ONE OF TOXIC CASCADE
NEUROTOXIC PROTEINS ARE LOWERED

Data from first 14 AD and PD patients





Aβ42/Aβ40 RATIO IN AD AND PD PATIENTS

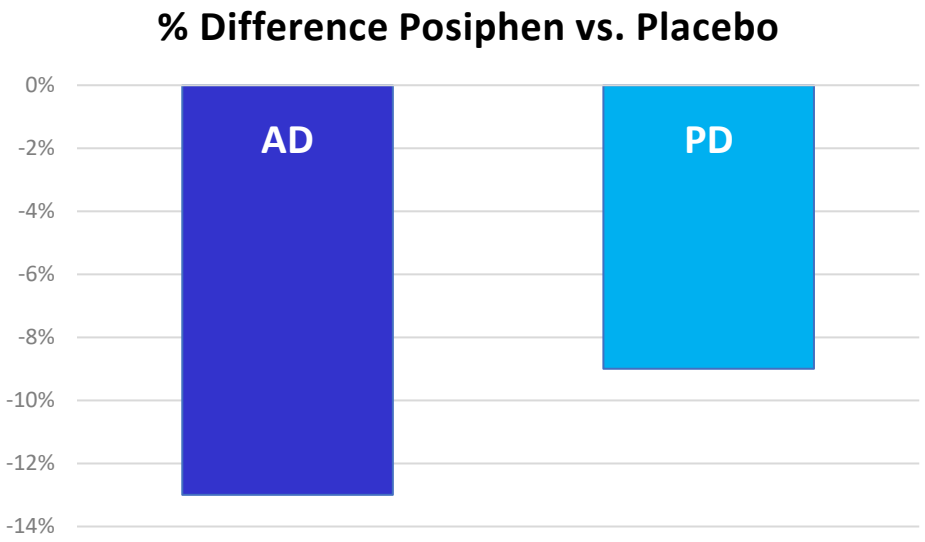
Data from first 14 AD and PD patients

	AD Patients		PD Patients	
	Placebo	Posiphen	Placebo	Posiphen
Baseline	0.064	0.059	0.083	0.097
25 Days	0.064	0.062	0.083	0.097
p-Value		0.0113		

The Aβ42/Aβ40 is **< 0.072** in AD. Our ratios in fact show that AD patients have AD, while PD patients do not. It also shows that in ANVS401 treated patients one month of treatment improves the ratio in a statistically significant fashion.

STEP TWO OF TOXIC CASCADE
NEUROFILAMENT LIGHT IS LOWERED IN AD AND PD PATIENTS

Data from first 14 AD and PD patients



Neurofilament light represents the health of the axon and neuron.

In both Posiphen-treated patient populations, NfL is reduced representing better axonal health.

STEP THREE OF TOXIC CASCADE INFLAMMATION IS LOWER IN PD PATIENTS

Data from first 14 PD patients

Inflammatory Marker	Compared to Baseline or Placebo	% Change from Baseline or Placebo	p-Value
YKL40	within	-22.9	0.032
	between	-55.5	0.097
sTREM2	within	-17.1	0.0001
	between	-42.7	0.001
GFAp	within	-41.6	0.000001
	between	-28.4	0.013

The trial measured four inflammatory markers that are prevalent in the brains of AD and of PD patients.

Each of the inflammatory markers showed statistically significant reduction after 25 days of treatment with ANVS401 compared to baseline and compared to placebo.

WORK IN PROGRESS & SUMMARY

- We have finished treating the additional 40 PD patients and are expecting to complete all the biomarkers of the toxic cascade in the next two months.
- The reversal of the toxic cascade confirms and cements the data seen to date.
- Showing efficacy in AD and in PD patients by two different tests each and showing that the efficacy spans all areas of the ADAS-Cog and the UPDRS strengthens our conclusion that Posiphen is effective in both patient populations.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THANK YOU
Symbol: ANVS (NYSE American)