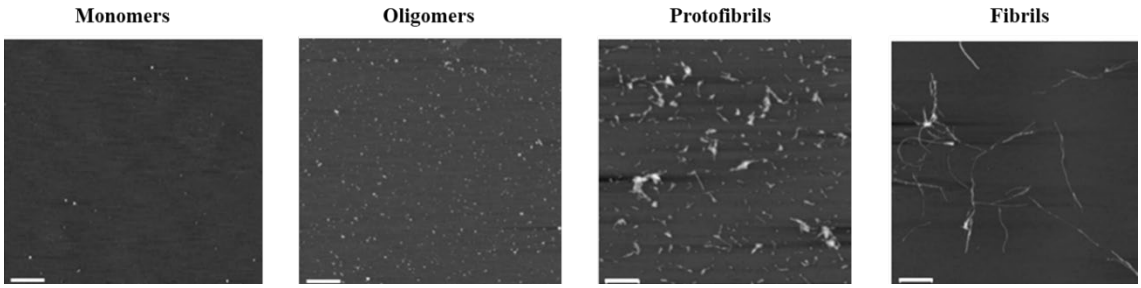
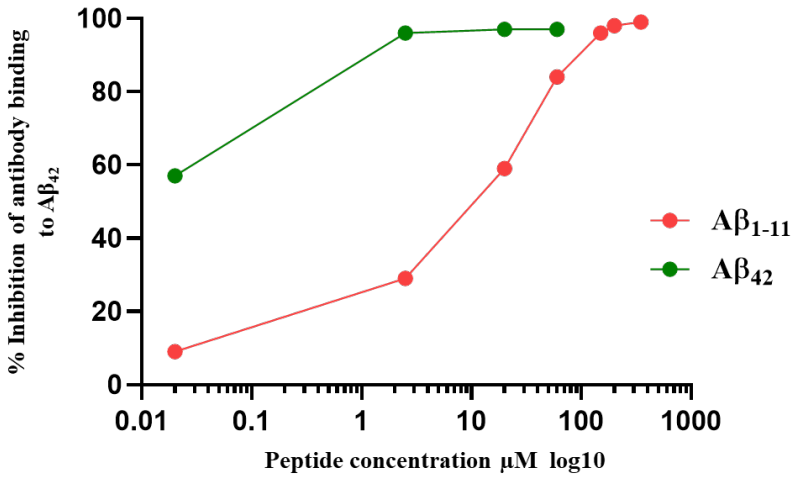
Supplementary Figures and Tables

Supplementary Table 1: Endpoint titers of anti-$A\beta_{42}$ antibodies in AV-1959R- and placebo-treated participants.

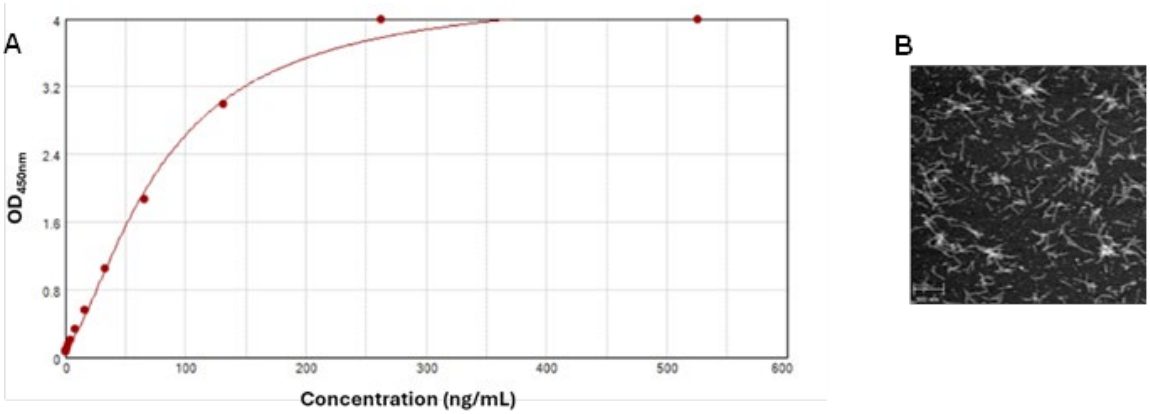
Rand #	Day 1	Day 42	Day 98	Day 112	Day 140	Day 154
Cohort 2 – 100 µg						
R001 (Placebo)	154	153	145	126	100	100
R002	100	35 625	5 354	12 757	5 333	4 480
R003 (Placebo)	100	100	100	100	100	100
R005	190	85 235	7 296	13 693	6 694	5 911
R006	269	42 728	9 634	36 951	19 911	16 951
R004	338	164 643	14 672	33 089	9 827	6 050
R007	203	63 707	7 855	25 112	12 628	10 176
R008	686	35 115	12 389	22 239	19 968	16 618
Cohort 2 – 300 µg						
R025	105	42 174	2 894	8 770	3 237	2 786
R026 (Placebo)	118	107	122	100	100	122
R027	100	64 924	12 558	13 169	9 115	6 556
R028 (Placebo)	109	124	135	117	108	281
R029	100	2 780	301	4 529	1 101	1 125
R038	157	92 632	19 520	23 885	12 467	11 359
R031	100	81 848	4 620	5 870	2 814	1 849
R032	167	78 281	8 733	12 513	6 769	5 278



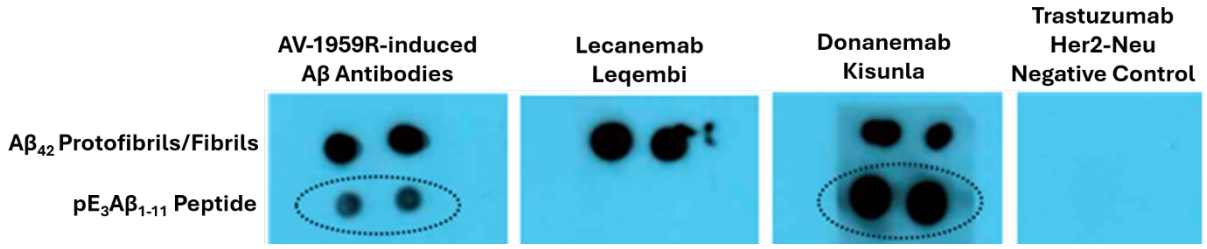
Supplementary Figure 1. Atomic Force Microscopy (AFM) images of $A\beta_{42}$ peptide conformers spotted onto microarray slides. scale bars are 500 nm.



Supplementary Figure 2. Competition ELISA demonstrating the specificity of vaccine-induced antibodies. Pre-incubation of pooled AV-1959R immune serum with soluble $A\beta_{42}$ peptide (2.5 µM) containing a protofibril/fibril mixture almost completely blocked binding to plate-bound $A\beta_{42}$, whereas approximately 150-200 µM of $A\beta_{1-11}$ peptide was required to achieve comparable inhibition. IC_{50} is 16.9 µM for $A\beta_{1-11}$ and 0.01 µM for the soluble $A\beta_{42}$ protofibril/fibril mixture.



Supplementary Figure 3. Affinity purification and concentration-dependent binding of AV-1959R–induced anti-Aβ antibodies with $Aβ_{42}$ protofibrils/fibrils. Aβ-specific antibodies were affinity-purified from pooled Day 42 immune sera of vaccinated participants. (A) Antibody concentration was determined, and binding to a mixture of $Aβ_{42}$ protofibrils and fibrils was evaluated by ELISA. (B) Atomic force microscopy (AFM) image of the $Aβ_{42}$ peptide preparation used for ELISA plate coating, showing a heterogeneous mixture of protofibrils and fibrils.



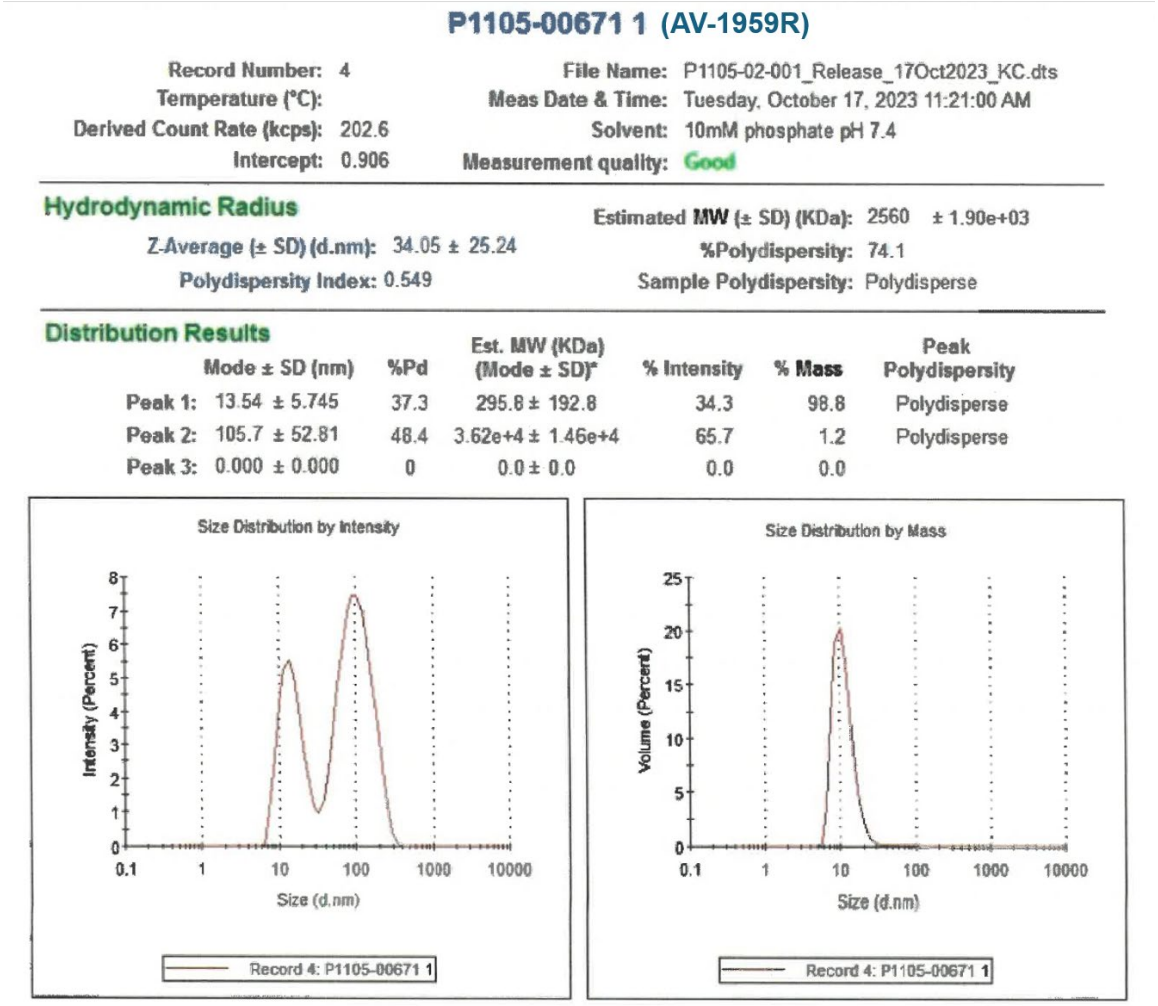
Supplementary Figure 4. Binding specificity of AV-1959R-induced antibodies compared with FDA-approved anti-amyloid monoclonal antibodies. Purified antibodies from AV-1959R-vaccinated participants were assessed by dot blot against $Aβ_{42}$ protofibrils/fibrils and pyroglutamate-modified $Aβ_{3-11}$ ($pE_3Aβ_{11}$). Vaccine-induced antibodies showed strong binding to fibrillar $Aβ_{42}$ and significant binding to $pE_3Aβ_{11}$. Lecanemab (Leqembi®) bound fibrillar $Aβ_{42}$ but not $pE_3Aβ_{11}$, whereas donanemab (Kisunla™) preferentially recognized $pE_3Aβ_{11}$. These findings demonstrate that AV-1959R elicits a polyclonal antibody repertoire that mirrors the clinically validated fibril-selective profile of lecanemab while extending coverage to pyroglutamate-modified $Aβ_{3-11}$ epitope, the N-terminal region of $pE_3Aβ_{42}$, which has been proposed to act as an early pathogenic aggregation seed.

Supplementary Table 2. Estimated values for *B1* (short-term) and *B2* (long-term) coefficients for both antibody peaks (priming and boosting).

Participant ID	B1-peak 1	B2-peak 1	B1-peak 2	B2-peak 2
R002	29572	6052	8003	4734
R004	151669	12973	28024	5088
R005	78964	6270	7037	6630
R006	30683	12044	16947	19989
R007	55443	8263	13229	11894
R008	18557	16557	2.98E-11	22518
R025	40138	2035	6028	2719
R027	49721	15202	4289	8964
R029	2481	298	3748	753
R031	79380	2467	3624	2269
R032	69495	8785	6107	6428
R038	68555	24076	10883	12945

Supplementary Table 3. Estimated time (number of days) to reach antibody titer 1:1000 after priming vaccination.

Participant ID	Days to 1:1000
R002	334
R004	458
R005	340
R006	445
R007	384
R008	497
R025	163
R027	483
R029	63
R031	191
R032	394
R038	558



Supplementary Figure 5. DLS profile of Purified AV-1959R protein, distribution by mass and intensity. 98.8% of particles are, on average, 13.54 ± 5.745 nm in diameter with a molecular weight of 295.8 ± 192.8 kDa, suggesting a uniform size distribution. The highly aggregated population (105.7 ± 52.81 nm, MW 3.62e+4 ± 1.46e+4) accounts for only 1.2% of the protein, and the signal is not visible in the mass distribution.