Supplementary Table 1. Risk of progression to CDR > 0 from multivariate Cox proportional hazards model with death as a competing risk.

	Hazard ratio[a]	95% CI	*P*-value
Preclinical biomarker (pos vs neg)	2.794	1.842-4.240	**<.0001**
Centered Age (with *APOE* ε4+)	1.052	1.008-1.097	**<.0001**
Centered Age (with *APOE* ε4-)	1.133	1.101-1.165	**<.0001**
APOE carrier (ε4+ vs ε4-)[b]	1.941	1.185-3.179	**p=0.0266** *APOE* alone
			p=0.0045 *APOE* x centered age interaction
Sex (female vs male)	0.976	0.629-1.513	0.9129
Self-reported race (NHW vs AA)	0.877	0.434-1.773	0.7152
Education[c]	0.997	0.907-1.095	0.9425
PRS	1.032	1.004-1.060	**0.0231**
Interval from baseline to final clinical assessment	0.972	0.912-1.037	0.3922

Abbreviations: AA = African-American; neg = negative; NHW = Non-Hispanic White; pos = positive; PRS = polygenic risk score;
[a]Analysis restricted to n=680 of total n=717 NHW and AA participants due to missing PRS values.
[b] At centered Age = -1.89699
[c] In centered years

Supplementary Table 2. Clinical characteristics of progressors (CDR >0) vs non-progressors (CDR = 0) in participants with longitudinal biomarkers

	Biomarker Negative Non-Progressors		**Biomarker Negative Progressors**			**Biomarker Positive Non-Progressors**		**Biomarker Positive Progressors**		
	n	Mean (SD) or %	*n*	Mean (SD) or %	p-value[a]	*n*	Mean (SD) or %	*n*	Mean (SD) or %	p-value[a]
Age, mean (SD), y	272	64.5 (8.6)	18	73.9 (9.4)	**<.0001**	44	69.8 (6.6)	18	72.2 (6.7)	0.1888
Male sex, %	96	35.3	8	44.4	0.4354	21	47.7	7	38.9	0.5287
APOE ε4 carriers, %	70	25.7	5	27.8	0.8493	26	59.1	12	66.7	0.5755
PRS, mean (SD)	272	-0.00355 (0.00682)	18	-0.00500 (0.00731)	0.3835	44	-0.00207 (0.00758)	18	-0.00221 (0.00802)	0.9493
Education, mean (SD), y	272	16.1 (2.5)	18	15.0 (2.4)	0.0731	44	16.2 (2.6)	18	15.0 (3.6)	0.1368
Interval from baseline assessment to final assessment, mean (SD), y	272	7.3 (3.0) {median=7.2}	18	7.3 (3.2) {median=8.1}	0.9796	44	6.7 (2.9) {median=6.0}	18	9.0 (2.8) {median=9.4}	**0.0076**
Interval from baseline biomarker to final biomarker, mean (SD), y	272	7.1 (3.0) {median=7.0}	18	7.1 (3.3) {median=7.6}	0.9472	44	6.7 (2.9) {median=5.8}	18	8.7 (2.8) {median=9.2}	**0.0131**
No. defined by CSF biomarker, %	8	6.6	1	5.6	0.5353	0	-	1	5.6	-
Baseline p-tau181/Aβ42, mean (SD)	8	0.0108 (0.0029)	1	0.0095	0.6823	0	-	1	0.0469	-
Final p-tau181/ Aβ42, mean (SD)	8	0.0142 (0.0088)	1	0.0103	0.6884	0	-	1	0.1118	-
No. defined by PET, %	264	97.1	17	94.4	0.5353	44	100	17	94.4	0.1141
Baseline PIB SUVR, mean (SD)	238	1.0254 (0.0956)	14	1.0268 (0.0988)	0.9584	40	2.1144 (0.5398)	17	2.5836 (0.7872)	**0.0118**
Final PIB SUVR, mean (SD)	69	1.1428 (0.2650)	10	1.1559 (0.1783)	0.8807	11	2.5670 (0.6051	8	2.9998 (0.3767)	0.0930
Baseline AV45 SUVR, mean (SD)	26	0.9658 (0.1662)	3	0.9417 (0.2684)	0.8233	4	2.0505 (0.3053)	0		-
Final AV45 SUVR, mean (SD)	185	1.0123 (0.2875)	5	0.9328 (0.2307)	0.5410	30	2.1639 (0.6068)	8	2.5570 (0.6295)	0.1148
Baseline Centiloid, mean (SD)	264	-2.0829 (5.7076)	17	-2.8839 (8.1490)	0.6949	44	48.9123 (24.0596)	17	68.7615 (35.4251)	**0.0448**
Final Centiloid, mean (SD)	253	-3.0721 (17.6139)	15	-0.6147 (12.7160)	0.5953	41	68.0816 (35.3633)	16	90.9494 (30.3974)	**0.0337**
No. converted from biomarker negative to positive, %[b]	27	9.93%	1	5.56%	0.5419					

Data only include the subset of participants with at least one additional biomarker assessment of the same modality used to define original biomarker status

Abbreviations: Aβ = amyloid-beta; AV45 = florbetapir (^{18}F-AV-45); CDR = Clinical Dementia Rating; PIB = Pittsburgh compound B; p-tau181 = tau phosphorylated at position 181; PRS = polygenic risk score; SUVR = standardized uptake value ratio;.

[a] p-values derived from tests comparing mean or % values between non-progressor and progressor subgroups for biomarker-negative and biomarker-positive participants

[b] The average interval between first and final biomarker assessment for biomarker converters was 8.1 years for non-progressors and 6.5 years for the single progressor

Supplementary Table 3. Neuropathological diagnoses of progressors (CDR >0) vs non-progressors (CDR = 0) by biomarker status.

	Biomarker-Negative Non-Progressors		Biomarker-Negative Progressors		Biomarker-Positive Non-Progressors		Biomarker-Positive Progressors	
	n	Mean (SD) or %	*n*	Mean (SD) or %	*n*	Mean (SD) or %	*n*	Mean (SD) or %
Age, mean (SD), y	18	76.8 (7.2)	17	81.3 (7.0)	7	74.9 (7.2)	15	80.3 (5.2)
Male sex, %	8	44.4	9	52.9	2	28.6	6	40.0
APOE ε4 carriers, %	3	16.7	1	5.9	3	42.9	7	46.7
Interval from baseline biomarker to death, mean (SD), y	18	5.7 (3.0)	17	7.9 (3.2)	7	5.0 (2.4)	15	8.5 (3.0)
Diagnosis, %								
Int-High ADNC[a]	0	0	3	17.6	5	71.4	15	100
Any Vascular Disease[b]	16	88.9	17	100	7	100	14	93.3
Substantial Vascular Disease[c]	7	38.9	7	41.2	0	0	9	60.0
Cerebral Lewy Body[d]	1	5.6	4	23.5	1	14.3	3	20.0
Hippocampal Sclerosis	0	6.9	3	17.6	0	0	0	0
Primary tauopathy[e]	10[f]	55.6	8[g]	47.1	0	0	7[h]	46.7
FTLD – TDP	0	0	1	5.9	0	0	0	0
Other	4[i]	22.2	3[j]	17.6	3[k]	42.9	7[l]	46.7

Abbreviations: ADNC = Alzheimer's disease neuropathological change; ARTAG = aging-related tau astrogliopathy; AGD = argyrophilic grain disease; CTE = chronic traumatic encephalopathy; CBD = corticobasal degeneration; Int-High = Intermediate-to-high; FTDP-17 = frontotemporal dementia and parkinsonism with tau linked to chromosome 17; FTLD = frontotemporal lobar degeneration; GGT = globular glial tauopathy; LATE-NC = limbic-predominant age-associated TDP-43 encephalopathy neuropathologic change; MTL = medial temporal lobe; PART = primary age-related tauopathy; PiD = Pick disease; PSP = progressive supranuclear palsy; TDP = TAR DNA binding protein 43 (TDP-43);

[a]Defined by NIA-Reagan intermediate-to-high likelihood of AD or NIA-AA intermediate-to-high ADNC

[b]Defined by presence of remote infarcts, hemorrhages, microinfarcts, cerebral microbleeds, any arteriolosclerosis, any white matter rarefaction, subcortical arteriolosclerotic leukoencephalopathy, amyloid angiopathy or other pathologic change related to ischemic or vascular disease

[c]Defined by presence of remote micro/macroinfarcts, remote hemorrhages, severe arteriolosclerosis, severe white matter rarefaction, or subcortical,arteriolosclerotic leukoencephalopathy

[d]Defined by presence of Lewy body pathology in limbic or neocortical regions

[e]Defined by presence of tau pathology consistent with PiD, CBD, PSP, FTDP-17, AGD, tangle-dominant disease/PART, other 4R tauopathies (including GGT and *MAPT* mutation tauopathies) or other 3R+4R tauopathies (including ARTAG, focal tauopathies, MAPT mutation tauopathies or other unclassifiable tauopathies)

[f] Primary tauopathy pathologies: FTDP-17 (n=1), AGD (n=6), tangle-dominant disease/PART (n=5), other 3R+4R tauopathy (n=5)

[g] Primary tauopathy pathologies: AGD (n=5), other 4R tauopathy (n=1), other 3R+4R tauopathy (n=4)

[h] Primary tauopathy pathologies: CBD (n=1), AGD (n=1), other 4R tauopathy (n=2) other 3R+4R tauopathy (n=4)

[i] Other pathologies: TDP-MTL/LATE-NC (n=2), primary neoplasm (n=2), metastatic neoplasm (n=2)

[j] Other pathologies: Prion disease (n=1), hypertrophic olivary degeneration (n=1), metastatic neoplasm (n=1)

[k] Other pathologies: Metabolic storage disease (n=1), demyelinating disease (n=1), heterotopia (n=1)

[l] Other pathologies: TDP-MTL/LATE-NC (n=2), prion disease (n=1), putative amygdala Lewy neurites (n=1), primary neoplasm (n=1), arachnoid cyst of caudate (n=1)