Many convergent orogens such as the eastern European Alps display an asymmetric doubly-vergent wedge geometry. Loci of deepest exhumation are located above the overriding retro-wedge, whereas increased fault activity occurs in the pro-wedge on the subducting plate. The main drainage divide separates steeper from more gently sloping topography on the two wedges of different critical taper. We performed apatite and zircon (U-Th)/He analyses densely spaced along the TRANSALP geophysical transect in combination with thermo-kinematic models based on cross-section balancing. Our new low temperature thermochronology data and thermo-kinematic model results underline (i) deepest levels of exhumation across the Tauern Window until the Pliocene and (ii) higher Late Neogene exhumation rates south of the Periadriatic Fault relative to the north, while seismic activity is focussed across the Southern Alps. Our proposed mantle-to-surface link positions the retro-wedge north of the Periadriatic Fault subsequent to subduction polarity reversal during continental collision. Present-day drainage divide migration trends and imaged locations of mantle-lithospheric slabs beneath TRANSALP suggest ongoing, slow slab reversal since Adriatic indentation in the Eastern Alps.