analysis). Between wk24 and wk48, response rates across disease measures were either sustained (e.g. SRI-4, 62% at wk24 vs 63% at wk48; joint response 87% at wk24 vs 87% at wk48) or increased (CLASI response, 53% at wk24 vs 69% at wk48) in those randomized to UST. Following crossover at wk 24, an additional 10%–20% of PBO patients responded to UST (n=33) in the outcomes studied. Clinical response to UST was associated with decreases in IFN- protein and gene signature. In contrast, IFN-I levels were stable over time and were not associated with UST response. Safety events were consistent with the known UST safety profile.

Conclusions UST provided sustained clinical benefit in global and organ (mucocutaneous and joint disease)-specific SLE activity measures with a safety profile consistent with approved indications. Thus, UST may be an effective biologic therapy for SLE by blocking IL-12 and IL-23-driven pathogenic mechanisms which are independent of the IFN-I pathway.

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TARGETED SEQUENCING IN 1200 SLE PATIENTS REVEAL DAP1 REGULATORY HAPLOTYPE THAT POTENTIATE AUTOIMMUNITY

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Abstract 202 Figure 1 SLE associated DAP1 haplotype in Caucasian, African American and Asian population. Panel a: shows the sequencing depth across DAP1 gene locus on chromosome 5. Panel b: shows the 62kb LD (Linkage Disequilibrium) block that contain top 19 SLE associated variants (rsIDs shown). The peak SLE associated SNP rs267985 and strongest DAP1 eQTL rs2930047 are shown. Panel c: Median-joining (MJ) network analysis on most common DAP1 haplotypes in Caucasian SLEs and healthy controls. Spheres (termed nodes) represent the locations of each haplotype (from Table 2) within the network and the size of the node is proportional to the overall frequency of that haplotype in the dataset. Each node is overlaid with a pie chart that reflects the frequency of that haplotype in SLE group (yellow) versus healthy group (black). The lines connecting the nodes are labeled with the variants that distinguish the connected nodes and the length is proportional to the number of variants. Odds ratio (OR) are shown for two most significant alleles. Red highlighted nodes indicate SLE risk clades. . Panel d: Median-joining (MJ) network analysis on most common DAP1 haplotypes in African American SLEs and healthy controls. . Panel e: Median-joining (MJ) network analysis on most common DAP1 haplotypes in Asian SLEs and healthy controls.