

## 2. STRUCTURE

### 2.1. REGN2222

REGN2222 (IgG1 isotype) is a covalent heterotetramer consisting of two disulfide-linked human heavy chains, each covalently linked through a disulfide bond to a fully human kappa light chain. Based on the primary sequence, the antibody without glycans possesses a predicted molecular weight of 145,797.7 Da, assuming the formation of 16 canonical disulfide bonds and removal of Lys<sup>453</sup> from each heavy chain C-terminus. There is a single N-linked glycosylation site (Asn<sup>303</sup>) on each heavy chain, located within the constant region in the Fc domain of the molecule. The variable domains of the heavy and light chains combine to form the complementarity-determining regions (CDRs) for the binding of REGN2222 to its target, RSV-F [respiratory syncytial virus fusion protein].

The amino acid sequence, CDRs, glycosylation site, and disulfide bond structures of REGN2222 monoclonal antibody are presented in [Figure 1](#).

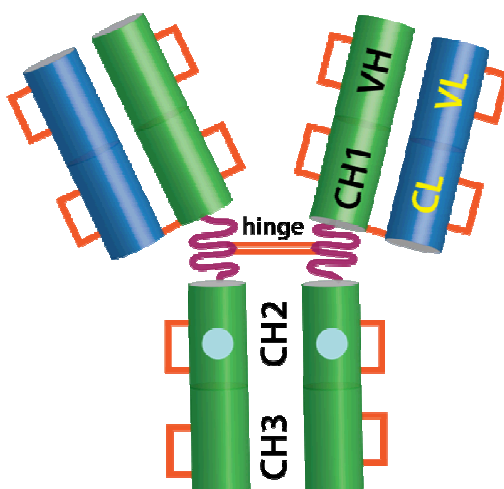
**Figure 1: Amino Acid Sequence and Schematic Representation of REGN2222****REGN2222 Heavy Chain**

EVQLVESGGD LVQPGRSLRL SCVASGFTFD DYAMHWVRQA PGKGLEWVSG VSWGSGSTV<sup>60</sup>  
 ADSVKGRFTV SRDNAQKSLY LQMNSLRAED TALYYCVKDA YKFNYYYGL DVWGQGT<sup>120</sup>  
 VSSASTKGPS VFPLAPSSKS TSGGTAALGC LVKDYFPEPV TVSWNSGALT SGVHTFPAVL<sup>180</sup>  
 QSSGLYSLSS VVTVPSSSLG TQTYICNVNH KPSNTKVDKK VEPKSCDKTH TCPPCPAPEL<sup>240</sup>  
 LGGPSVFLFP PKPKDTLMIS RTPEVTCVVV DVSHEDPEVK FNWYVDGVEV HNAKTKPREE<sup>300</sup>  
 QYNSTYRVVS VLTVLHQDWL NGKEYKCKVS NKALPAPIEK TISKAKGQPR EPQVYTLPPS<sup>360</sup>  
 RDELTKNQVS LTCLVKGFYP SDIAVEWESN GPENNYKTT PPVLDSGDSF FLYSKLTVDK<sup>420</sup>  
 SRWQQGNVFS CSVMHEALHN HYTQKSLSL PGK<sup>453</sup>

CPPC of HC

**REGN2222 Light Chain**

EIVMTQSPAT LSVSPGERAT LSCRASQTIL SNLAWYLQKP GQAPRLLIYG ASSTRATGLPA<sup>60</sup>  
 RFSGSGSGTE FTLTISSLQS EDFAVYYCQQ YNNWPLTFGG GTKVEIKRTV AAPSVFIFPP<sup>120</sup>  
 SDEQLKSGTA SVVCLLNNFY PREAKVQWKV DNALQSGNSQ ESVTEQDSKD STYLSLSTLT<sup>180</sup>  
 LSKADYEKHK VYACEVTHQG LSSPVTKSFN RGE<sup>214</sup>



**Top:** REGN2222 antibody amino acid sequence with post-translational modifications denoted. The sequences of REGN2222 heavy chain and light chain CDR regions are highlighted in blue. The cysteine residues (red) that have been confirmed to form predicted disulfide bonds are connected by solid orange lines. The Fc N-linked glycosylation site at Asn<sup>303</sup> is highlighted in green. The heavy chain C-terminal Lys<sup>453</sup> (pink) is predominantly removed during manufacture. **Bottom:** Representation of the structure of REGN2222 depicting the location of each of the intra-chain and inter-chain disulfide bonds (orange). Heavy (green) and light chains (blue) are connected by inter-chain disulfide bonds; heavy chain dimerization is achieved through two heavy chain intermolecular disulfide bonds located within the hinge region. The Fc domain glycosylation site is also indicated (cyan).