What is claimed is:

1. A bi-functional fusion protein comprising a first domain and a second domain, wherein

the first domain is capable of binding to AREG or a fragment thereof, preferably is an antibody or an antigen-binding fragment thereof that binds to AREG or a fragment thereof, and

the second domain is capable of binding to a TGFβ ligand or a fragment thereof, preferably comprises a part of the ectodomain of TGFβ receptor II (TRII) or a variant thereof.

2. The bi-functional fusion protein of claim 1, wherein the antibody or the antigen-binding fragment thereof is capable of binding to both human AREG and mouse AREG, alternatively, the anti-AREG antibody or the fragment thereof is capable of binding to human AREG with weak or without cross-reactivity to mouse AREG, and/or

wherein the anti-AREG antibody or the fragment thereof is a human anti-AREG antibody, a murine anti-AREG antibody, a chimeric anti-AREG antibody, or a humanized anti-AREG antibody, preferably, is a human monoclonal antibody (mAb), murine mAb, chimeric mAb or humanized mAb, and/or

wherein the anti-AREG antibody or the fragment thereof is capable of binding to a soluble form of AREG, preferably, is capable of binding to an epidermal growth factor (EGF)-like domain of the soluble form of AREG.

3. The bi-functional fusion protein of claim 1, wherein the anti-AREG antibody or the fragment thereof comprises a heavy chain variable region comprising heavy chain complementarity determining regions HCDR1, HCDR2, and HCDR3, and a light chain variable region comprising light chain complementarity determining regions LCDR1, LCDR2, and LCDR3, wherein:

HCDR1, HCDR2, and HCDR3 are selected from a group consisting of:

(1) HCDR1: SYAMS (SEQ ID NO: 1), HCDR2: AISGSGGSTYYADSVKG (SEQ ID NO: 2), HCDR3: PTSRYSYGYDY (SEQ ID NO: 3);

(2) HCDR1: SYAMS (SEQ ID NO: 1), HCDR2: AISGSGGSTYYADSVKG (SEQ ID NO: 2), HCDR3: PTSRYSYSYNN (SEQ ID NO: 4);

(3) HCDR1: SHAMS (SEQ ID NO: 5), HCDR2: AISGSGGSTYYADSVKG (SEQ ID NO: 2), HCDR3: VDTKFDP (SEQ ID NO: 6);

(4) HCDR1: SYPMS (SEQ ID NO: 7), HCDR2: TISTGGTYTYYPDSVKG (SEQ ID NO: 8), HCDR3: QGPIYYGNYYYAMDY (SEQ ID NO: 9);

(5) HCDR1: SYPMS (SEQ ID NO: 7), HCDR2: TISTGGRYTYYPDSVKG (SEQ ID NO: 10), HCDR3: QGPIYYGNYYYAMDY (SEQ ID NO: 9);

(6) HCDR1: SYPMS (SEQ ID NO: 7), HCDR2: TISTGGTYTYYPDSVKG (SEQ ID NO:

8), HCDR3: QGPILRKNYYYGMDV (SEQ ID NO: 11);

(7) HCDR1: SYPMS (SEQ ID NO: 7), HCDR2: TISTGGTYTYYPDSVKG (SEQ ID NO: 8), HCDR3: QGPIYYGNYYYGMDV (SEQ ID NO: 12);

(8) HCDR1: SYAMS (SEQ ID NO: 1), HCDR2: TISTGGSHTYYPDSVKG (SEQ ID NO: 13), HCDR3: HGYLLYDGYYEWYFDV (SEQ ID NO: 14);

(9) HCDR1: SYAMS (SEQ ID NO: 1), HCDR2: TISTGGSHTYYPDSVKG (SEQ ID NO: 13), HCDR3: HGYLLYDGYYEWYFDY (SEQ ID NO: 140);

(10) HCDR1: SYAMS (SEQ ID NO: 1), HCDR2: TISTGGSHTYYPESVKG (SEQ ID NO: 15), HCDR3: HGYLLYEGYYEWYFDY (SEQ ID NO: 16);

(11) HCDR1: GYPMS (SEQ ID NO: 17), HCDR2: TISTGARHTYYPDSVKG (SEQ ID NO: 18), HCDR3: HEGLRRGKYHCIMDY (SEQ ID NO: 19);

(12) HCDR1: GYPMS (SEQ ID NO: 17), HCDR2: TISTGARHTYYPDSVKG (SEQ ID NO: 18), HCDR3: HEGLRRGKYHSIMDY (SEQ ID NO: 20); and

(13) HCDR1, HCDR2, HCDR3 as shown in (1)-(12), but at least one of which includes one, two, three, four or five amino acids addition, deletion, conservative amino acid substitution or the combinations thereof; and

LCDR1, LCDR2, and LCDR3 are selected from a group consisting of:

(1) LCDR1: TGNSNNVGDQGAV (SEQ ID NO: 21), LCDR2: RNNNRPS (SEQ ID NO: 22), LCDR3: STWDSGLNSVV (SEQ ID NO: 23);

(2) LCDR1: TGNSNNVGDQGAV (SEQ ID NO: 21), LCDR2: RNNNRPS (SEQ ID NO: 22), LCDR3: STWDKNNKSVV (SEQ ID NO: 24);

(3) LCDR1: SGSSSNIGSNTVN (SEQ ID NO: 25), LCDR2: SNNQRPS (SEQ ID NO: 26), LCDR3: EVWDDSLNGPV (SEQ ID NO: 27);

(4) LCDR1: RSSQSLVHSDGNTYLH (SEQ ID NO: 28), LCDR2: KVSNRFS (SEQ ID NO: 29), LCDR3: SQSTHVPYT (SEQ ID NO: 30);

(5) LCDR1: RSSQSLVDGEDGTYLN (SEQ ID NO: 31), LCDR2: KVSERFD (SEQ ID NO: 32), LCDR3: SQSTHVPYT (SEQ ID NO: 30);

(6) LCDR1: RSSQSLVDGQDGTYLH (SEQ ID NO: 33), LCDR2: KVSNRFD (SEQ ID NO: 34), LCDR3: SQSTHVPYT (SEQ ID NO: 30);

(7) LCDR1: RSSQSLVNQEGETYLH (SEQ ID NO: 35), LCDR2: KVSNRFD (SEQ ID NO: 34), LCDR3: SQSTHVPYT (SEQ ID NO: 30);

(8) LCDR1: KASQSVDYDGHSFLN (SEQ ID NO: 36), LCDR2: AASNLES (SEQ ID NO: 37), LCDR3: QQSTEDPPYT (SEQ ID NO: 38);

(9) LCDR1: RASESVDYDGHSFIN (SEQ ID NO: 39), LCDR2: AASNKDT (SEQ ID NO: 40), LCDR3: QQSTEDPPYT (SEQ ID NO: 38);

(10) LCDR1: RASQSVDYDGHSFLN (SEQ ID NO: 41), LCDR2: AASNLQS (SEQ ID

NO: 42), LCDR3: QQSTEDPPYT (SEQ ID NO: 38);

(11) LCDR1: KSSQSVDYDGHSFLN (SEQ ID NO: 43), LCDR2: AASNRES (SEQ ID NO: 44), LCDR3: QQSTEDPPYT (SEQ ID NO: 38);

(12) LCDR1: RASESVDYDGHSFIN (SEQ ID NO: 39), LCDR2: AASNKDT (SEQ ID NO: 40), LCDR3: QQSTEDPPYT (SEQ ID NO: 38);

(13) LCDR1: RASQSVDYEGHSFLN (SEQ ID NO: 45), LCDR2: AASNLQS (SEQ ID NO: 42), LCDR3: QQSTENPPYT (SEQ ID NO: 46);

(14) LCDR1: KSSQSVDYEGHSFLN (SEQ ID NO: 47), LCDR2: AASNRES (SEQ ID NO: 44), LCDR3: QQSTENPPYT (SEQ ID NO: 46);

(15) LCDR1: KASQSIDYDGDSFLN (SEQ ID NO: 48), LCDR2: AASNLES (SEQ ID NO: 37), LCDR3: HQCNEDPYM (SEQ ID NO: 49);

(16) LCDR1: RASESVDYDGDSFIN (SEQ ID NO: 50), LCDR2: AASNKDT (SEQ ID NO: 40), LCDR3: HQSNEDPYM (SEQ ID NO: 51);

(17) LCDR1: RASESVDYDGDSFIN (SEQ ID NO: 50), LCDR2: AASNKDT (SEQ ID NO: 40), LCDR3: HQSNEDPYL (SEQ ID NO: 52);

(18) LCDR1: RASESVDYDGDSFIN (SEQ ID NO: 50), LCDR2: AASNKDT (SEQ ID NO: 40), LCDR3: HQSNEDPYV (SEQ ID NO: 53);

(19) LCDR1: RASQSIDYDGDSFLN (SEQ ID NO: 54), LCDR2: AASNLQS (SEQ ID NO: 42), LCDR3: QQSNEDPYV (SEQ ID NO: 55);

(20) LCDR1: KSSQSIDYDGDSFLN (SEQ ID NO: 56), LCDR2: AASNRES (SEQ ID NO: 44), LCDR3: QQSNEDPYV (SEQ ID NO: 55); and

(21) LCDR1, LCDR2, LCDR3 as shown in (1)-(20), but at least one of which includes one, two, three, four or five amino acids addition, deletion, conservative amino acid substitution or the combinations thereof.

4. The bi-functional fusion protein of claim 1, wherein the anti-AREG antibody or a fragment thereof comprises a heavy chain variable region comprising heavy chain complementarity determining regions HCDR1, HCDR2, and HCDR3, and a light chain variable region comprising light chain complementarity determining regions LCDR1, LCDR2, and LCDR3, wherein:

HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, and LCDR3 are selected from a group consisting of:

(1) HCDR1: SYAMS (SEQ ID NO: 1), HCDR2: AISGSGGSTYYADSVKG (SEQ ID NO: 2), HCDR3: PTSRYSYGYDY (SEQ ID NO: 3), LCDR1: TGNSNNVGDQGAV (SEQ ID NO: 21), LCDR2: RNNNRPS (SEQ ID NO: 22), LCDR3: STWDSGLNSVV (SEQ ID NO: 23);

(2) HCDR1: SYAMS (SEQ ID NO: 1), HCDR2: AISGSGGSTYYADSVKG (SEQ ID NO: 2), HCDR3: PTSRYSYSYNN (SEQ ID NO: 4), LCDR1: TGNSNNVGDQGAV (SEQ ID NO:

21), LCDR2: RNNNRPS (SEQ ID NO: 22), LCDR3: STWDKNNKSVV (SEQ ID NO: 24);

(3) HCDR1: SHAMS (SEQ ID NO: 5), HCDR2: AISGSGGSTYYADSVKG (SEQ ID NO: 2), HCDR3: VDTKFDP (SEQ ID NO: 6), LCDR1: SGSSSNIGSNTVN (SEQ ID NO: 25), LCDR2: SNNQRPS (SEQ ID NO: 26), LCDR3: EVWDDSLNGPV (SEQ ID NO: 27);

(4) HCDR1: SYPMS (SEQ ID NO: 7), HCDR2: TISTGGTYTYYPDSVKG (SEQ ID NO: 8), HCDR3: QGPIYYGNYYYAMDY (SEQ ID NO: 9), LCDR1: RSSQSLVHSDGNTYLH (SEQ ID NO: 28), LCDR2: KVSNRFS (SEQ ID NO: 29), LCDR3: SQSTHVPYT (SEQ ID NO: 30);

(5) HCDR1: SYPMS (SEQ ID NO: 7), HCDR2: TISTGGRYTYYPDSVKG (SEQ ID NO: 10), HCDR3: QGPIYYGNYYYAMDY (SEQ ID NO: 9), LCDR1: RSSQSLVDGEDGTYLN (SEQ ID NO: 31), LCDR2: KVSERFD (SEQ ID NO: 32), LCDR3: SQSTHVPYT (SEQ ID NO: 30);

(6) HCDR1: SYPMS (SEQ ID NO: 7), HCDR2: TISTGGTYTYYPDSVKG (SEQ ID NO: 8), HCDR3: QGPILRKNYYYGMDV (SEQ ID NO: 11), LCDR1: RSSQSLVDGQDGTYLH (SEQ ID NO: 33), LCDR2: KVSNRFD (SEQ ID NO: 34), LCDR3: SQSTHVPYT (SEQ ID NO: 30);

(7) HCDR1: SYPMS (SEQ ID NO: 7), HCDR2: TISTGGTYTYYPDSVKG (SEQ ID NO: 8), HCDR3: QGPIYYGNYYYGMDV (SEQ ID NO: 12), LCDR1: RSSQSLVNQEGETYLH (SEQ ID NO: 35), LCDR2: KVSNRFD (SEQ ID NO: 34), LCDR3: SQSTHVPYT (SEQ ID NO: 30);

(8) HCDR1: SYAMS (SEQ ID NO: 1), HCDR2: TISTGGSHTYYPDSVKG (SEQ ID NO: 13), HCDR3: HGYLLYDGYYEWYFDV (SEQ ID NO: 14), LCDR1: KASQSVDYDGHSFLN (SEQ ID NO: 36), LCDR2: AASNLES (SEQ ID NO: 37), LCDR3: QQSTEDPPYT (SEQ ID NO: 38);

(9) HCDR1: SYAMS (SEQ ID NO: 1), HCDR2: TISTGGSHTYYPDSVKG (SEQ ID NO: 13), HCDR3: HGYLLYDGYYEWYFDY (SEQ ID NO: 140), LCDR1: RASESVDYDGHSFIN (SEQ ID NO: 39), LCDR2: AASNKDT (SEQ ID NO: 40), LCDR3: QQSTEDPPYT (SEQ ID NO: 38);

(10) HCDR1: SYAMS (SEQ ID NO: 1), HCDR2: TISTGGSHTYYPDSVKG (SEQ ID NO: 13), HCDR3: HGYLLYDGYYEWYFDY (SEQ ID NO: 140), LCDR1: RASQSVDYDGHSFLN (SEQ ID NO: 41), LCDR2: AASNLQS (SEQ ID NO: 42), LCDR3: QQSTEDPPYT (SEQ ID NO: 38);

(11) HCDR1: SYAMS (SEQ ID NO: 1), HCDR2: TISTGGSHTYYPDSVKG (SEQ ID NO: 13), HCDR3: HGYLLYDGYYEWYFDY(SEQ ID NO: 140), LCDR1: KSSQSVDYDGHSFLN (SEQ ID NO: 43), LCDR2: AASNRES (SEQ ID NO: 44), LCDR3: QQSTEDPPYT (SEQ ID NO: 38);

(12) HCDR1: SYAMS (SEQ ID NO: 1), HCDR2: TISTGGSHTYYPESVKG (SEQ ID NO: 15), HCDR3: HGYLLYEGYYEWYFDY (SEQ ID NO: 16), LCDR1: RASESVDYDGHSFIN (SEQ ID NO: 39), LCDR2: AASNKDT (SEQ ID NO: 40), LCDR3: QQSTEDPPYT (SEQ ID NO: 38);

(13) HCDR1: SYAMS (SEQ ID NO: 1), HCDR2: TISTGGSHTYYPESVKG (SEQ ID NO: 15), HCDR3: HGYLLYEGYYEWYFDY (SEQ ID NO: 16), LCDR1: RASQSVDYEGHSFLN (SEQ ID NO: 45), LCDR2: AASNLQS (SEQ ID NO: 42), LCDR3: QQSTENPPYT (SEQ ID NO: 46);

(14) HCDR1: SYAMS (SEQ ID NO: 1), HCDR2: TISTGGSHTYYPESVKG (SEQ ID NO: 15), HCDR3: HGYLLYEGYYEWYFDY (SEQ ID NO: 16), LCDR1: KSSQSVDYEGHSFLN (SEQ ID NO: 47), LCDR2: AASNRES (SEQ ID NO: 44), LCDR3: QQSTENPPYT (SEQ ID NO: 46);

(15) HCDR1: GYPMS (SEQ ID NO: 17), HCDR2: TISTGARHTYYPDSVKG (SEQ ID NO: 18), HCDR3: HEGLRRGKYHCIMDY (SEQ ID NO: 19), LCDR1: KASQSIDYDGDSFLN (SEQ ID NO: 48), LCDR2: AASNLES (SEQ ID NO: 37), LCDR3: HQCNEDPYM (SEQ ID NO: 49);

(16) HCDR1: GYPMS (SEQ ID NO: 17), HCDR2: TISTGARHTYYPDSVKG (SEQ ID NO: 18), HCDR3: HEGLRRGKYHSIMDY (SEQ ID NO: 20), LCDR1: RASESVDYDGDSFIN (SEQ ID NO: 50), LCDR2: AASNKDT (SEQ ID NO: 40), LCDR3: HQSNEDPYM (SEQ ID NO: 51);

(17) HCDR1: GYPMS (SEQ ID NO: 17), HCDR2: TISTGARHTYYPDSVKG (SEQ ID NO: 18), HCDR3: HEGLRRGKYHSIMDY (SEQ ID NO: 20), LCDR1: RASESVDYDGDSFIN (SEQ ID NO: 50), LCDR2: AASNKDT (SEQ ID NO: 40), LCDR3: HQSNEDPYL (SEQ ID NO: 52);

(18) HCDR1: GYPMS (SEQ ID NO: 17), HCDR2: TISTGARHTYYPDSVKG (SEQ ID NO: 18), HCDR3: HEGLRRGKYHSIMDY (SEQ ID NO: 20), LCDR1: RASESVDYDGDSFIN (SEQ ID NO: 50), LCDR2: AASNKDT (SEQ ID NO: 40), LCDR3: HQSNEDPYV (SEQ ID NO: 53);

(19) HCDR1: GYPMS (SEQ ID NO: 17), HCDR2: TISTGARHTYYPDSVKG (SEQ ID NO: 18), HCDR3: HEGLRRGKYHSIMDY (SEQ ID NO: 20), LCDR1: RASQSIDYDGDSFLN (SEQ ID NO: 54), LCDR2: AASNLQS (SEQ ID NO: 42), LCDR3: QQSNEDPYV (SEQ ID NO: 55);

(20) HCDR1: GYPMS (SEQ ID NO: 17), HCDR2: TISTGARHTYYPDSVKG (SEQ ID NO: 18), HCDR3: HEGLRRGKYHSIMDY (SEQ ID NO: 20), LCDR1: KSSQSIDYDGDSFLN (SEQ ID NO: 56), LCDR2: AASNRES (SEQ ID NO: 44), LCDR3: QQSNEDPYV (SEQ ID NO: 55); and

(21) HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, LCDR3 as shown in (1)-(20), but at least one of which includes one, two, three, four or five amino acids addition, deletion, conservative amino acid substitution or the combinations thereof.

5. The bi-functional fusion protein of claim 1, wherein the anti-AREG antibody or the fragment thereof comprises a heavy chain variable region, and a light chain variable region, wherein the heavy chain variable region has an amino acid sequence selected from a group consisting of SEQ ID NOs: 57-69, and an amino acid sequence having at least 95% sequence

identity to any one of SEQ ID NOs: 57-69, and retaining epitope-binding activity,

wherein the light chain variable region has an amino acid sequence selected from a group consisting of SEQ ID NOs: 70-89, and an amino acid sequence having at least 95% sequence identity to any one of SEQ ID NOs: 70-89, and retaining epitope-binding activity.

6. The bi-functional fusion protein of claim 1, wherein the anti-AREG antibody or the fragment thereof comprises a heavy chain variable region, and a light chain variable region, wherein the heavy chain variable region and the light chain variable region have an amino acid sequences selected from the group consisting of:

(1) SEQ ID NO: 57 and SEQ ID NO: 70;

(2) SEQ ID NO: 58 and SEQ ID NO: 71;

(3) SEQ ID NO: 59 and SEQ ID NO: 72;

(4) SEQ ID NO: 60 and SEQ ID NO: 73;

(5) SEQ ID NO: 61 and SEQ ID NO: 74;

(6) SEQ ID NO: 62 and SEQ ID NO: 75;

(7) SEQ ID NO: 63 and SEQ ID NO: 76;

(8) SEQ ID NO: 64 and SEQ ID NO: 77;

(9) SEQ ID NO: 65 and SEQ ID NO: 78;

(10) SEQ ID NO: 66 and SEQ ID NO: 79;

(11) SEQ ID NO: 66 and SEQ ID NO: 80;

(12) SEQ ID NO: 66 and SEQ ID NO: 81;

(13) SEQ ID NO: 67 and SEQ ID NO: 79;

(14) SEQ ID NO: 67 and SEQ ID NO: 82;

(15) SEQ ID NO: 67 and SEQ ID NO: 83;

(16) SEQ ID NO: 68 and SEQ ID NO: 84;

(17) SEQ ID NO: 69 and SEQ ID NO: 85;

(18) SEQ ID NO: 69 and SEQ ID NO: 86;

(19) SEQ ID NO: 69 and SEQ ID NO: 87;

(20) SEQ ID NO: 69 and SEQ ID NO: 88;

(21) SEQ ID NO: 69 and SEQ ID NO: 89; and

(22) two amino acid sequences having at least 95% sequence identity to any one of (1)-(21) respectively, and retaining epitope-binding activity.

7. The bi-functional fusion protein of claim 1, wherein the anti-AREG antibody or the fragment thereof is an isotype of IgG, IgM, IgA, IgE, IgD or a variant thereof, preferably, an isotype of IgG1, IgG2, IgG3, IgG4 or a variant thereof.

8. The bi-functional fusion protein of claim 1, wherein the second domain comprises the ectodomain of TRII or a variant thereof, preferably the variant comprises a site mutation, and/or a deletion,

preferably the ectodomain of TRII has an amino acid sequence shown in SEQ ID NO: 90, or an amino acid sequence that is at least 85% identical to SEQ ID NO: 90.

9. The bi-functional fusion protein of claim 8, wherein the site mutation comprises one or more site mutations at position(s) selected from K7, T16, D17, R34, R66, K67, K103, and K104 on the basis of the numbering of SEQ ID NO: 90 from N-terminus to C-terminus,

preferably the site mutation comprises one or more site mutations selected from K7Q, T16S, D17N, R34S, R34H, R66S, K67S, K103S, and K104S on the basis of the numbering of SEQ ID NO: 90 from N-terminus to C-terminus,

more preferably the site mutation is selected from: T16S and D17N; K7Q and D17N; K7Q; R34S; R34H; R66S and K67S; K103S and K104S; K7Q and R34S; K7Q, R66S and K67S; K7Q, K103S, and K104S; K7Q, R34S, R66S, and K67S; K7Q, R34S, K103S, and K104S; K7Q, R66S, K67S, K103S, and K104S; R34S, R66S, K67S, K103S, and K104S; K7Q, R34S, R66S, K67S, K103S, and K104S.

10. The bi-functional fusion protein of claim 8, wherein the variant has an N-terminus deletion of four to twenty-one amino acids, preferably, four amino acids, seven amino acids, nine amino acids, thirteen amino acids, seventeen amino acids, and twenty-one amino acids, on the basis of the numbering of SEQ ID NO: 90 from N-terminus to C-terminus.

11. The bi-functional fusion protein of claim 8, wherein the variant comprises site mutations T16S and D17N, and an N-terminus deletion of seven amino acids.

12. The bi-functional fusion protein of claim 8, wherein the second domain comprises the ectodomain of TRII or a variant thereof and has an amino acid sequence as shown in any one of SEQ ID NOs: 90-107, or an amino acid sequence having at least 85% identity to any one of SEQ ID NOs: 90-107.

13. The bi-functional fusion protein of claim 3, wherein C-terminus of a heavy chain or a

light chain of the anti-AREG antibody is fused with N-terminus of the ectodomain of TRII or its variant directly, or via a linker; or N-terminus of a heavy chain or a light chain of the anti-AREG antibody is connected with C-terminus of the ectodomain of TRII or its variant directly, or via a linker,

preferably the bi-functional fusion protein comprises: a heavy chain of the anti-AREG antibody, at its N-terminus, connected with C-terminus of the ectodomain of TRII or its variant directly, or via a linker; or, a heavy chain of the anti-AREG antibody, at its C-terminus, connected with N-terminus of the ectodomain of TRII or its variant directly, or via a linker,

preferably the bi-functional fusion protein further comprises a light chain of the anti-AREG antibody, and/or the bi-functional fusion protein is in a form of heterotetramer.

14. The bi-functional fusion protein of claim 13, wherein the linker comprises a linker peptide shown by a formula $(G_4S)_n$, $(G_4S)_nG$, $S(G_4S)_nG$, $SG(EAAAK)_nSG$, $S(GEGES)_nG$, or $(EAAAK)_n$, wherein n is an integer of 1 to 5, preferably, the linker peptide has an amino acid sequence shown by any one of SEQ ID NOs: 108-117.

15. The bi-functional fusion protein of claim 1, wherein the bi-functional fusion protein comprises a heavy chain of the anti-AREG antibody, at its C-terminus, connected with N-terminus of the ectodomain of TRII via a linker, and has an amino acid sequence shown in any one of SEQ ID NOs: 118-139 and 142, or an amino acid sequence having at least 85% identity to any one of SEQ ID NOs: 118-139 and 142.

16. An isolated nucleic acid molecule, encoding the bi-functional fusion protein as defined in any one of claims 1-15.

17. An expression vector, comprising the isolated nucleic acid molecule of claim 16.

18. A host cell, which comprises the isolated nucleic acid molecule of claim 16, or the expression vector of claim 17.

19. A pharmaceutical composition, comprising the bi-functional fusion protein of any one of claims 1-15 and a pharmaceutically acceptable carrier.

20. The bi-functional fusion protein of any one of claims 1-15, the isolated nucleic acid of claim 16, or the pharmaceutical composition of claim 19 for use in the prevention, treatment and/or diagnosis of fibrotic diseases, cancers and diseases associated with chronic inflammation in a subject, preferably, the fibrotic diseases include renal fibrosis, hepatic fibrosis, pulmonary fibrosis, in particular, idiopathic pulmonary fibrosis (IPF).