of: a Fab fragment, a $F(ab')_2$ fragment, and a scFv fragment. In some examples, the antibody or fragment thereof is glycosylated. In some examples, the antibody or fragment thereof contains one or more complementary determining regions of the light or heavy chain of the antibody produced by the hybridoma deposited at the ATCC and designated by the Patent Deposit Designation PTA-10431 or PTA-10432. In some examples, the antibody is an antibody produced by the hybridoma deposited at the ATCC and designed by the Patent Deposit Designation PTA-10431, or an antigen-binding fragment thereof, or an antibody produced by the hybridoma deposited at the ATCC and designated by the Patent Deposit Designation PTA-10432, or an antigen-binding fragment thereof.

Also provided are isolated antibodies and antigen-binding fragments thereof that specifically bind to human soluble ST2, wherein the antibodies and antigen-binding fragments thereof were produced by a process that includes immunizing a non-human mammal (e.g., mouse, rat, rabbit, goat, cow, pig, monkey, or horse) with a recombinant human soluble ST2 isolated from a human cell (e.g., a human fibroblast, neuronal, epithelial, or endothelial cell, an embryonic or adult cell, especially a human embryonic kidney cell). In some examples, the recombinant human soluble ST2 isolated is fully glycosylated, i.e., has substantially the same glycosylation as a native endogenous human soluble ST2 present in human serum. In some examples of all of the antibodies and fragments described herein, the antibody or fragment thereof is labeled.

Also provided are cells of the hybridoma deposited at the ATCC and designated by the Patent Deposit Designation PTA-10431 and cells of the hybridoma deposited at the ATCC and designated by the Patent Deposit Designation PTA-10432.

In one aspect, the present disclosure refers to a method of identifying a subject as at risk of developing a cardiovascular disease, the method comprising:

determining a level of human soluble ST2 in a sample that has been obtained from the subject using an isolated antibody produced by the hybridoma deposited at the American Type Culture Collection (ATCC) and designated by the Patent Deposit Designation PTA-10431 or an antigen-binding fragment thereof,

wherein an elevated level of human soluble ST2 in the sample compared to a reference level of human soluble ST2 indicates that the subject is at risk of developing a cardiovascular disease.

In one aspect, the present disclosure refers to a method of identifying a subject as at risk of developing a cardiovascular disease, the method comprising:

determining a level of human soluble ST2 in a sample that has been obtained from the subject using an isolated antibody produced by the hybridoma deposited at the American Type Culture Collection (ATCC) and designated by the Patent Deposit Designation PTA-10432 or an antigen-binding fragment thereof,

wherein an elevated level of human soluble ST2 in the sample compared to a reference level of human soluble ST2 indicates that the subject is at risk of developing a cardiovascular disease.

Also provided are methods of quantitating a level of human soluble ST2 in a sample from a subject. The methods include contacting the sample with at least one antibody or fragment thereof described herein, and detecting binding of the antibody or fragment thereof to human soluble ST2. In some examples, the method includes the use of at least two different antibodies or fragments thereof described herein.

Also provided are methods of predicting the risk of death within one year in a subject. The methods include obtaining a sample from a subject and determining the

subject using at least one antibody or fragment thereof described herein, wherein the subject's level of human soluble ST2 relative to a reference level of human soluble ST2 is used to select a therapeutic treatment for the subject. In some examples, the presence of an elevated level of human soluble ST2 is used to select the therapeutic treatment for the subject.

In one aspect, the present disclosure refers to a method of selecting a therapeutic treatment for a subject, the method comprising:

determining a level of human soluble ST2 in a sample that has been obtained from the subject using (i) an isolated antibody produced by the hybridoma deposited at the American Type Culture Collection (ATCC) and designated by Patent Deposit Designation PTA-10432, or an antigen-binding fragment of an antibody produced by the hybridoma deposited at the ATCC and designated by Patent Deposit Designation PTA-10432; and (ii) an isolated antibody produced by the hybridoma deposited at the American Type Culture Collection (ATCC) and designated by Patent Deposit Designation PTA-10431, or an antigen-binding fragment of an antibody produced by the hybridoma deposited at the ATCC and designated by Patent Deposit Designation PTA-10431, identifying a subject having an elevated level of human soluble ST2 in the sample compared to a reference level of human soluble ST2 as a subject in need of the therapeutic treatment; and selecting a therapeutic treatment for the subject.

In one aspect, the present disclosure refers to a method of selecting a therapeutic treatment for a subject, the method comprising:

determining a level of human soluble ST2 in a sample that has been obtained from the subject using an isolated antibody produced by the hybridoma deposited at the American Type Culture Collection (ATCC) and designated by the Patent Deposit Designation PTA-10432 or an antigen-binding fragment thereof,

identifying a subject having an elevated level of human soluble ST2 in the sample compared to a reference level of human soluble ST2 as a subject in need of the therapeutic treatment; and

selecting a therapeutic treatment for the subject. In some examples of any of the methods described herein, the subject is undiagnosed or is not presenting with two or more (e.g., at least three, four, or five) symptoms of a disease state; the subject has been diagnosed as having a disease (e.g., heart failure, coronary artery disease, cardiovascular disease, acute coronary syndrome, renal insufficiency, stroke, or any of the diseases described herein); or the subject has one or more of: hypertriglyceridemia, hypercholesterolemia, hypertension, and a body mass index of ≥ 30. In some examples of any of the methods described herein, the determining is performed using at least two antibodies or fragments thereof described herein.

In some examples of any of the methods described herein, the reference level of human soluble ST2 is a threshold level of human soluble ST2. In some examples, the threshold level is an average level of human soluble ST2 in a healthy patient population (e.g., a healthy male patient population or a healthy female patient population). In some examples of any of the methods described herein, the reference level is a level of human soluble ST2 present in a sample of a subject not presenting with two or more symptoms of disease, a subject not diagnosed as having a disease, or a subject not identified as being at risk for developing a disease.

In any of the methods described herein, the subject has not been diagnosed as having a disease (e.g., heart failure, coronary artery disease, cardiovascular disease, acute coronary artery disease, acute coronary syndrome, renal insufficiency, or stroke, or any of the diseases described herein). In any of the methods described herein, the sample contains blood, serum, or plasma. Any of the antibodies and fragments thereof described herein can be used in any of methods described herein.

Also provided are methods of diagnosing a disease in a subject including obtaining a sample from a subject, determining a level of human soluble ST2 in the

sample using at least one antibody or fragment thereof described herein and a level of at least one additional marker, wherein an elevated level of human soluble ST2 in the sample compared to a reference level of human soluble ST2 and an altered level of the at least one additional marker relative to a reference level of the at least one additional marker, indicate that the subject has the disease (e.g., cardiovascular disease, a pulmonary disease, sepsis, Kawasaki disease, or a Th2-associated disease, or any of the other diseases described herein).

Also provided are methods for determining whether a subject has a normal human soluble ST2 level (and thus is likely to be free from severe disease, e.g., cardiovascular disease, and a normal risk of death or hospitalization, e.g., within one year) including obtaining a sample from a subject and determining the level of human soluble ST2 in the sample, wherein the subject is determined to have a normal human soluble ST2 level if the level of human soluble ST2 falls in a specific range (e.g., between about 14.5 to about 25.3 ng/mL, or between about 18.1 to about 19.9 ng/mL). In some examples, a male subject is determined to have a normal human soluble ST2 level if the level of human soluble ST2 is between any range listed in Table 9. In some examples, a female subject is determined to have a normal human soluble ST2 if the level of human soluble ST2 is between any range listed in Table 9.

In one aspect, the present disclosure refers to a method of determining whether a subject has a normal soluble ST2 level, the method comprising:

determining a level of human soluble ST2 in a sample that has been obtained from the subject using using (i) an isolated antibody produced by the hybridoma deposited at the American Type Culture Collection (ATCC) and designated by Patent Deposit Designation PTA-10432, or an antigen-binding fragment of an antibody produced by the hybridoma deposited at the ATCC and designated by Patent Deposit Designation PTA-10432; and (ii) an isolated antibody produced by the hybridoma deposited at the American Type Culture Collection (ATCC) and designated by Patent Deposit Designation PTA-10431, or an antigen-binding fragment of an antibody produced by the hybridoma deposited at the ATCC and designated by Patent Deposit Designation PTA-10431, wherein the level of human soluble ST2 in the sample is determined to have a normal soluble ST2 level if the level of human soluble ST2 falls within the range of 14.5 ng/ml to 25.3 ng/ml.

In one aspect, the present disclosure refers to a method of determining whether a subject has a normal soluble ST2 level, the method comprising:

determining a level of human soluble ST2 in a sample that has been obtained from the subject using an isolated antibody produced by the hybridoma deposited at the American Type Culture Collection (ATCC) and designated by the Patent Deposit Designation PTA-10432 or an antigen-binding fragment thereof,

wherein the level of human soluble ST2 in the sample is determined to have a normal human soluble ST2 level if the level of human soluble ST2 falls within the range of 14.5 ng/ml to 25.3 ng/ml.

Also provided are kits containing at least one (e.g., two, three, four, or five) of the antibodies or antigen-binding fragments thereof described herein. Some examples of these kits contain two antibodies or antigen-binding fragments thereof described herein. In some examples of these kits, at least one of the antibodies or fragments thereof has a K_D for binding to human soluble ST2 (e.g., recombinant human soluble ST2) equal to or less than 8.59×10^{-10} M. In some examples, the kit is provided as an enzyme-linked immunosorbent assay (ELISA). In some examples, the kit further contains a recombinant human soluble ST2 isolated from a human cell (e.g., a human embryonic kidney cell). In some examples, the recombinant human soluble ST2 is fully glycosylated.

By the term "soluble ST2" is meant a soluble protein containing a sequence at least 90% identical (e.g., at least 95%, 96%, 97%, 98%, 99%, or 100% identical) to NCBI

WHAT IS CLAIMED IS:

1. A method of determining prognosis in a subject having heart failure or myocardial infarction, the method comprising:

determining a level of human soluble ST2 in a sample that has been obtained from the subject using an isolated antibody produced by the hybridoma deposited at the American Type Culture Collection (ATCC) and designated by the Patent Deposit Designation PTA-10431 or an antigen-binding fragment thereof,

wherein an elevated level of human soluble ST2 in the sample compared to a reference level of human soluble ST2 indicates a poor prognosis of heart failure or myocardial infarction in the subject.

2. A method of determining prognosis in a subject having heart failure or myocardial infarction, the method comprising:

determining a level of human soluble ST2 in a sample that has been obtained from the subject using an isolated antibody produced by the hybridoma deposited at the American Type Culture Collection (ATCC) and designated by the Patent Deposit Designation PTA-10432 or an antigen-binding fragment thereof,

wherein an elevated level of human soluble ST2 in the sample compared to a reference level of human soluble ST2 indicates a poor prognosis of heart failure or myocardial infarction in the subject.

3. A method of selecting a therapeutic treatment for a subject, the method comprising:

determining a level of human soluble ST2 in a sample that has been obtained from the subject using (i) an isolated antibody produced by the hybridoma deposited at the American Type Culture Collection (ATCC) and designated by Patent Deposit Designation PTA-10432, or an antigen-binding fragment of an antibody produced by the hybridoma deposited at the ATCC and designated by Patent Deposit Designation PTA-10432; and (ii) an isolated antibody produced by the hybridoma deposited at the American Type Culture Collection (ATCC) and designated by Patent

Deposit Designation PTA-10431, or an antigen-binding fragment of an antibody produced by the hybridoma deposited at the ATCC and designated by Patent Deposit Designation PTA-10431,

identifying a subject having an elevated level of human soluble ST2 in the sample compared to a reference level of human soluble ST2 as a subject in need of the therapeutic treatment; and

selecting a therapeutic treatment for the subject.

4. A method of selecting a therapeutic treatment for a subject, the method comprising:

determining a level of human soluble ST2 in a sample that has been obtained from the subject using an isolated antibody produced by the hybridoma deposited at the American Type Culture Collection (ATCC) and designated by the Patent Deposit Designation PTA-10432 or an antigen-binding fragment thereof,

identifying a subject having an elevated level of human soluble ST2 in the sample compared to a reference level of human soluble ST2 as a subject in need of the therapeutic treatment; and

selecting a therapeutic treatment for the subject.

5. The method of claim 3 or 4, wherein the therapeutic treatment is selected from the group consisting of: nitrates, calcium channel blockers, diuretics, thrombolytic agents, digitalis, renin-angiotensin-aldosterone system (RAAS) modulating agents, and cholesterol-lowering agents.

6. The method of any one of claims 3-5, wherein the reference level of human soluble ST2 is an average level of human soluble ST2 in a healthy population.

7. The method of claim 6, wherein the healthy population is a healthy male population.

8. The method of claim 6, wherein the healthy population is a healthy female population.

9. The method of any one of claims 3-5, wherein the reference level is a level of human soluble ST2 present in a sample of a subject not presenting with two or more symptoms of a cardiovascular disease.

10. The method of any one of claims 3-5, wherein the reference level is a level of human soluble ST2 present in a sample of a subject not diagnosed as having a disease.

11. A method of determining whether a subject has a normal soluble ST2 level, the method comprising:

determining a level of human soluble ST2 in a sample that has been obtained from the subject using (i) an isolated antibody produced by the hybridoma deposited at the American Type Culture Collection (ATCC) and designated by Patent Deposit Designation PTA-10432, or an antigen-binding fragment of an antibody produced by the hybridoma deposited at the ATCC and designated by Patent Deposit Designation PTA-10432; and (ii) an isolated antibody produced by the hybridoma deposited at the American Type Culture Collection (ATCC) and designated by Patent Deposit Designation PTA-10431, or an antigen-binding fragment of an antibody produced by the hybridoma deposited at the ATCC and designated by Patent Deposit Designation PTA-10431,

wherein the level of human soluble ST2 in the sample is determined to have a normal soluble ST2 level if the level of human soluble ST2 falls within the range of 14.5 ng/ml to 25.3 ng/ml.

12. A method of determining whether a subject has a normal soluble ST2 level, the method comprising:

determining a level of human soluble ST2 in a sample that has been obtained from the subject using an isolated antibody produced by the hybridoma deposited at the

American Type Culture Collection (ATCC) and designated by the Patent Deposit Designation PTA-10432 or an antigen-binding fragment thereof,

wherein the level of human soluble ST2 in the sample is determined to have a normal human soluble ST2 level if the level of human soluble ST2 falls within the range of 14.5 ng/ml to 25.3 ng/ml.

13. The method of claim 11 or 12, wherein a normal soluble ST2 level in the subject indicates that the subject is likely to be free from severe disease and has a normal risk of death or hospitalization within one year.

14. A method of identifying a subject as at risk of developing a cardiovascular disease, the method comprising:

determining a level of human soluble ST2 in a sample that has been obtained from the subject using an isolated antibody produced by the hybridoma deposited at the American Type Culture Collection (ATCC) and designated by the Patent Deposit Designation PTA-10431 or an antigen-binding fragment thereof,

wherein an elevated level of human soluble ST2 in the sample compared to a reference level of human soluble ST2 indicates that the subject is at risk of developing a cardiovascular disease.

15. A method of identifying a subject as at risk of developing a cardiovascular disease, the method comprising:

determining a level of human soluble ST2 in a sample that has been obtained from the subject using an isolated antibody produced by the hybridoma deposited at the American Type Culture Collection (ATCC) and designated by the Patent Deposit Designation PTA-10432 or an antigen-binding fragment thereof,

wherein an elevated level of human soluble ST2 in the sample compared to a reference level of human soluble ST2 indicates that the subject is at risk of developing a cardiovascular disease.

16. The method of claim 14 or 15, wherein the cardiovascular disease is heart failure or coronary artery disease.

17. The method of any one of claims 3, 4, and 14-16, wherein the subject is undiagnosed or is not presenting with two or more symptoms of a cardiovascular disease.

18. The method of any one of claims 3, 4, and 14-16, wherein the subject has one or more of: hypertriglyceridemia, hypercholesterolemia, hypertension, and a body mass index of ≥ 30.

19. The method of any one of claims 3, 4, and 14-16, wherein the subject has one or more of the following symptoms: chest pain or discomfort, shortness of breath, nausea, vomiting, eructation, sweating, palpitations, lightheadedness, fatigue, and fainting.

20. The method of any one of claims 1-19, wherein the sample comprises blood, serum, or plasma.

21. The method of any one of claims 1-20, wherein the antigen-binding fragment is a Fab fragment or a $F(ab')_2$ fragment.

22. The method of any one of claims 1-20, wherein the antibody or the antigen-binding fragment is glycosylated.

23. The method of any one of claims 1-20, wherein the antibody or the antigen-binding fragment is labeled.