CLAIMS

What is claimed is:

1. A method of identifying a subject with myelodysplastic syndrome (MDS) for treatment with a telomerase inhibitor, the method comprising:

measuring hTERT expression level in a biological sample obtained previously from the subject after administration of a telomerase inhibitor; and

comparing the hTERT expression level in the biological sample to a baseline hTERT expression level prior to administration of the telomerase inhibitor;

wherein a reduction in hTERT expression level in the biological sample after administration of the telomerase inhibitor identifies a subject who has an increased likelihood of benefiting from treatment with the telomerase inhibitor, and

wherein the telomerase inhibitor is imetelstat or a pharmaceutically acceptable salt thereof.

2. The method of claim 1, wherein the reduction in hTERT expression level is 50% or more.

3. The method of any one of claims 1-2, wherein the subject is diagnosed as having trisomy 8.

4. The method of claim 3, wherein the subject is diagnosed as having trisomy 8 with mosaicism.

5. The method of any one of claims 3-4, further comprising diagnosing the subject with trisomy 8.

6. A method of treating myelodysplastic syndrome (MDS), the method comprising:

classifying a subject as having a reduction in hTERT expression level in a biological sample of target cells after administration of the telomerase inhibitor as compared to a baseline expression level prior to administration of the telomerase inhibitor, wherein a reduction in hTERT expression level in the biological sample after administration of the telomerase inhibitor

identifies the subject as having an increased likelihood of benefiting from treatment with the telomerase inhibitor; and

administering to the subject in need thereof an effective amount of a telomerase inhibitor, and

wherein the telomerase inhibitor is imetelstat or a pharmaceutically acceptable salt thereof.

7. The method of claim 6, wherein the hTERT expression level is reduced by 50% or more relative to a baseline hTERT expression level prior to administration of the telomerase inhibitor.

8. The method of claim 6 or 7, further comprising altering the dosage of the telomerase inhibitor, the frequency of dosing, or the course of therapy administered to the subject.

9. The method of any one of claims 6-8, wherein the subject is diagnosed as having trisomy 8.

10. The method of claim 9, wherein the subject is diagnosed as having trisomy 8 with mosaicism.

11. The method of any one of claims 9-10, further comprising diagnosing the subject with trisomy 8.

12. A method of monitoring therapeutic efficacy in a subject with myelodysplastic syndrome (MDS), the method comprising:

measuring hTERT expression level in a biological sample obtained from the subject after administration of a telomerase inhibitor; and

comparing the hTERT expression level in the biological sample to a baseline hTERT expression level prior to administration of the telomerase inhibitor;

wherein a 50% or greater reduction in hTERT expression level in the biological sample after administration of the telomerase inhibitor identifies a subject who has an increased likelihood of benefiting from treatment with the telomerase inhibitor, and

wherein the telomerase inhibitor is imetelstat or a pharmaceutically acceptable salt thereof.

13. The method of any one of claims 1-12, wherein the hTERT expression level measured or assessed is hTERT RNA expression level.

14. The method of any one of claims 1-12, wherein the hTERT expression level measured or assessed is hTERT protein expression level.

15. The method of any one of claims 1-14, wherein the subject is naive to treatment with an agent selected from a hypomethylating agent (HMA), lenalidomide, and combination thereof.

16. The method of any one of claims 1-15, wherein the MDS is relapsed or refractory MDS.

17. The method of any one of claims 1-16, wherein the MDS is MDS relapsed/refractory to erythropoiesis-stimulating agent (ESA).

18. The method of any one of claims 1-17, wherein the subject is classified as a low or intermediate-1 IPSS risk MDS subject.

19. The method of any one of claims 1-18, wherein the subject is transfusion dependent.

20. The method of claim 19, wherein the transfusion dependent subject has a transfusion requirement of about 4 units or more during the 8 weeks prior to the administration of the telomerase inhibitor.

21. The method of any one of claims 1-20, wherein the subject is a non-del5q human patient.

22. The method of any one of claims 1-21, wherein the subject is naive to treatment with lenalidomide.

23. The method of any one of claims 1-21, wherein the subject is naive to treatment with HMA selected from decitabine and azacitidine.

24. The method of any one of claims 1-23, wherein the imetelstat is imetelstat sodium.

25. The method of claim 24, wherein the telomerase inhibitor is administered for 1, 2, 3, 4, 5, 6, 7, 8 or more than 8 dosage cycles, each cycle comprising:

(a) intravenous administration of about 7-10 mg/kg imetelstat once every four weeks;

(b) intravenous administration of about 7-10 mg/kg imetelstat once weekly for four weeks;

(c) intravenous administration of about 2.5-10 mg/kg imetelstat once every three weeks; or

(d) intravenous administration of about 0.5-9.4 mg/kg imetelstat once every four weeks.

26. The method of claim 25, wherein each dosage cycle comprises intravenous administration of about 7-10 mg/kg imetelstat once every four weeks.

27. The method of claim 1, wherein the MDS is relapsed or refractory MDS and wherein the subject is classified as a low or intermediate-1 IPSS risk MDS subject.

28. The method of claim 27, wherein the subject is transfusion dependent.

29. The method of claim 27, wherein the subject is a non-del5q human patient.

30. The method of any one of claims 1-29, wherein the subject is naive to treatment with an agent selected from a hypomethylating agent (HMA) and lenalidomide.

31. The method of any one of claims 12-30, wherein the subject is diagnosed as having trisomy 8.

32. The method of claim 31, wherein the subject is diagnosed as having trisomy 8 with mosaicism.

33. The method of any one of claims 31-32, further comprising diagnosing the subject with trisomy 8.

34. Use of a telomerase inhibitor in the treatment of a subject with myelodysplastic syndrome (MDS), wherein a biological sample obtained from the subject is determined to have a reduction in hTERT expression level after administration of the telomerase inhibitor as compared to a baseline hTERT expression level in a biological sample obtained from the subject prior to administration of the telomerase inhibitor, wherein the reduction in hTERT expression level in the biological sample after administration of the telomerase inhibitor identifies the subject as having an increased likelihood of benefiting from treatment with the telomerase inhibitor, and

wherein the telomerase inhibitor is imetelstat or a pharmaceutically acceptable salt thereof.