1. **SUPPLEMENTAL NOTES. Detailed clinical histories of selected patients with t-AML/t-MDS harboring *TP53* mutations**

2. **SUPPLEMENTARY TABLE 1. Clinical, cytogenetic, and recurrent mutation information on 111 t-AML/t-MDS patients either sequenced by WGS or by targeted sequencing**

3. **SUPPLEMENTARY TABLE 2. Structural variants in 22 t-AML WGS patients**

4. **SUPPLEMENTARY TABLE 3. Validated SNVs and tier 1 insertions or deletions in 22 t-AML patients identified by WGS sequencing**

5. **SUPPLEMENTARY TABLE 4. 149 genes targeted for extension sequencing in 89 t-AML/t-MDS patients**

6. **SUPPLEMENTARY TABLE 5. Validated SNVs and tier 1 insertions or deletions in 89 t-AML/t-MDS patients identified by targeted sequencing**

7. **SUPPLEMENTARY TABLE 6. Statistically significant univariate correlations between cytogenetic and mutational markers in 111 t-AML/t-MDS patients**

8. **SUPPLEMENTARY TABLE 7. Cytogenetic and mutational markers with a statistically significant effect on overall survival by multivariate analysis in 52 t-AML or 59 t-MDS patients**

9. **SUPPLEMENTARY TABLE 8. SNVS and indels identified in UPN 967645 by exome sequencing**

10. **SUPPLEMENTARY TABLE 9. Whole genome sequencing coverage in 22 t-AML patients**

11. **SUPPLEMENTARY TABLE 10. Targeted sequencing coverage in 89 t-AML/t-MDS patients**

12. **SUPPLEMENTARY TABLE 11. Primers used in read-family NGS experiments**

SUPPLEMENTAL NOTES

Detailed clinical histories of selected patients with t-AML/t-MDS harboring *TP53* mutations

UPN 530447. At the age of 30, this patient was diagnosed with stage IVB Hodgkin's disease (nodular sclerosing type) with involvement of his retroperitoneal lymph nodes, spleen, and bone marrow. He received ABVD (doxorubicin, bleomycin, vinblastine, and dacarbazine) x 6 cycles with a partial response. As salvage therapy, he received MOPP (nitrogen mustard, vincristine, procarbazine, and prednisone) x 4 cycles followed by an autologous stem cell transplant with total body irradiation (1200 cGy), cyclophosphamide, and etoposide conditioning. Four years after achieving complete remission, he relapsed with bone marrow involvement. He received EVAP (etoposide, vinblastine, doxorubicin, and prednisolone) x 7 cycles with a good response and clearance of his bone marrow. He relapsed again one year later. A bone marrow biopsy at this time showed a normal karyotype with no lymphoma involvement and no evidence of myelodysplasia. He received four cycles of nitrogen mustard, vincristine, and dexamethasone followed by four cycles of vincristine, cyclophosphamide, and dexamethasone. He also received radiation to his right iliopsoas region for loco-regional control. He was consolidated with an autologous stem cell transplant with BEAM (BCNU, etoposide, cytarabine, and melphalan) conditioning. The leukapharesis sample used in this study was obtained at this time. Six years after his second autologous stem cell transplant, he presented with worsening fatigue, fever, anemia, thrombocytopenia, and leukocytosis. He was noted to have a peripheral blood blast count of 26%. A bone marrow biopsy was diagnostic for AML with a 40% blasts and complex cytogenetics including del5q and del7. Clonal biallelic mutations of *TP53* were identified. He was induced with cytarabine and idarubicin. However, he went into septic shock and died on day+8 of induction chemotherapy.

UPN 341666. This patient was diagnosed with stage IA diffuse large B-cell lymphoma at the age of 38. He did not have bone marrow involvement. He received CHOP (cyclophosphamide, vincristine, doxorubicin, and prednisone) x 3 cycles and radiation to his left neck. Three months after completion of therapy, he presented with mental status changes and was noted to have a 4.5 x 4.2 cm thalamic mass. He received 5 cycles of procarbazine, ritixumab, vincristine, and intrathecal methotrexate. He was consolidated with an autologous stem cell transplant with cyclophosphamide and total body irradiation conditioning. The leukapheresis sample used in this study was obtained at this time. He went into remission following his autologous stem cell transplant. He presented three years later with anemia and thrombocytopenia. A bone marrow biopsy showed evidence of myelodysplastic syndrome (RAEB-1) with complex cytogenetics including del7. He underwent a matched unrelated donor transplant (busulfan and cytoxan conditioning). He never experienced full count recovery after his transplant, and he died of complications from liver failure secondary to acute GVHD.

UPN 967645. At age 49, this patient was diagnosed with a marginal zone lymphoma by bone marrow biopsy. Peripheral blood flow cytometry showed no abnormalities. No treatment was pursued. One year later, he was noted to be pancytopenic. Another bone marrow biopsy was performed, which again showed involvement by a low-grade B cell lymphoproliferative disorder. At this time, his prior banked flow cytometry bone marrow sample was obtained. Again, no treatment was pursued. Due to worsening pancytopenia, treatment was initiated one year later. He received 6 cycles of fludarabine, achieving a complete remission with his mid-treatment bone marrow biopsy revealing a hypocellular marrow with trilineage hematopoiesis and no evidence of involvement by the B cell lymphoma. He received no further treatment. Four years later, a bone marrow biopsy performed for persistent pancytopenia revealed AML with 21% blasts and complex cytogenetics. He received decitabine x 1 with no improvement in his blood counts. He died of pneumonia two months after his AML diagnosis.

UPN 895681. At age 61, this patient was diagnosed with a stage 1A DLBCL with a 4 x 4 x 2 cm left inguinal mass. As part of his staging workup, he had a bone marrow biopsy performed, which showed tri-lineage hematopoiesis with no evidence of involvement by the DLBCL. The FFPE specimen of the core biopsy was banked at this time. He underwent CHOP (cyclophosphamide, vincristine, doxorubicin, and prednisone) x 3 cycles followed by field radiation to his left inguinal region. Approximately 1.5 years later, he relapsed with extensive periaortic, retroperitoneal, and mesenteric adenopathy. He received 3 cycles of salvage R-DHAP (rituximab, dexamethasone, doxorubicin, cisplatin, cytarabine) and was consolidated with an autologous stem cell transplant (BCNU, etoposide, cytarabine, and melphalan conditioning). Approximately 3.5 years, later, he was diagnosed with MDS with del7. He underwent several rounds of treatment including azacytidine x 4 cycles, PXD-101 (a histone-deacetylase inhibitor) x 8 cycles, and decitabine/arsenic x 3 cycles. His MDS was banked 2 years after its diagnosis. He progressed to AML 3 years after his initial MDS diagnosis and died 3 months later.