Shwachman-Diamond Syndrome (SDS) is an autosomal recessive disorder characterized by exocrine pancreatic insufficiency, neutropenia, short stature and skeletal abnormalities. Individuals with SDS possess a greatly increased risk of developing myelodysplastic syndrome (MDS) and acute myeloid leukemia (AML). Epidemiologic studies suggest that the lifetime risk of developing MDS/AML is ~30%. Approximately 90% of SDS cases are caused by mutations in the Shwachman–Bodian–Diamond syndrome (SBDS) gene. SBDS is a single member of a highly conserved protein family involved in ribosome biogenesis. To our knowledge, we established the first zebrafish model of SDS that phenocopies human Shwachman-Diamond Syndrome: neutropenia, atrophy in pancreas, liver and digestive tract, this one also showed lower cell proliferation. We also found activation of Tp53 pathway. Our results make it a highly relevant model to investigate its pathophysiology and develop new small molecule therapies. Based on our zebrafish model, we hypothesize that defects in sbds causes an activation of Tp53, cell cycle arrest, and apoptosis.