EXHIBIT A
1. I am submitting this report in connection with claims brought by Mr. Edwin Hardeman regarding his non-Hodgkin lymphoma. A copy of my curriculum vitae is attached as Ex. A and a copy of materials I considered is attached as Ex. B. These references are representative of the pertinent scientific literature but they do not represent the total of my professional experience and I do not necessarily agree with each of the statements made in these references. Information regarding my fees for work in this matter as well as a listing of my previous testimony is set forth in Exhibit C. A list of case-specific medical records I reviewed is attached as Exhibit D.

2. I reviewed pathology slides from Mr. Hardeman as follows: 7 slides from the neck fine needle aspiration (SRON15-116); 11 slides from the bone marrow aspirate, clot section and biopsy (SROS13-2923); and 5 slides containing no tissue from a needle biopsy (SROS15-2109). No immunohistochemical studies related to any of these specimens were received for review. I reserve the right to provide further comment upon review of the immunohistochemical studies for any of the specimens or of slides containing actual tissue for SROS15-2109 up to and including the time of trial.

3. I am an internationally recognized hematopathologist, researcher and educator, and an authority on the diagnosis and classification of lymphoma. I currently hold the position of Donald West and Mary Elizabeth King Professor and Chair of Pathology at the University of Chicago Medical School. Prior to joining the University of Chicago, from 2012-2016, I was at Stanford University, where I was the Ronald F. Dorfman Professor of Hematopathology, vice chair for clinical services, senior associate chair for hematopathology and medical director of anatomic pathology and clinical laboratory services. My research focuses on molecular genetic and immunophenotypic changes in hematopoietic tumors. I co-authored changes to the 2016 World Health Organization (WHO) classification of hematopoietic and lymphoid neoplasms, including the incorporation of genetic changes, and was the lead author of a summary of the 2016 WHO classification of myeloid neoplasms and acute leukemias published in Blood. I am the author of more than 300 professional scientific publications, book sections and chapters, and I have edited a number of textbooks in the field. My education, training, and professional qualifications are more fully described in Ex. A.

4. The opinions set forth in this report are held to a reasonable degree of scientific and medical certainty based on my education, training, experience, my review of the pathology, and my review of the relevant scientific and medical literature. They are held to the same standards that I utilize in my academic and clinical practice.

5. Non-Hodgkin lymphoma (NHL) is a group of malignant neoplasms (cancer) of lymphocytes that represent 4% of all new cancer cases each year an estimated 566,000 new cases
of lymphoma in 2012 (Stewart BW, Wild CP, editors. World Cancer Report 2014) and 74,680 in the US in 2018 (American Cancer Society Cancer Facts & Figures). Lymphocytes are composed of B-cells and T-cells and both types are involved in the normal immune response that assists in the body's response to infection. The majority of the body's lymphocytes are T-cells, but over 90% of cases of NHL derive from B-cells. B-cells function primarily to produce antibodies that are specific against antigens, often infectious organisms. In the normal state, a person exposed to an infectious agent has B-cells develop over a matter of days that can kill the infectious agent. Once these antigen specific B-cells are present in the body, they provide the person with a level of immunity if they become infected with that agent again so that they either do not become ill or they respond quickly to the illness. To develop such specificity, the B cell undergoes rearrangement of its genetic material (DNA) that allows it to develop antibodies specific for the infectious agent. This B-cell population expands during infection and then decreases when the infection is controlled. The process of gene rearrangement, however, sometimes results in non-productive reshuffling of the genetic material (DNA) that may include the acquisition of a genetic translocation. In most cases, because the genetic change is not productive for the cell, the cell dies; therefore, the abnormal genetic change has no impact on the individual. On rare occasions, the genetic event is retained in a living cell that divides and becomes, over time, a type of NHL.

6. There are at least 57 overall different types of B-cell NHL and at least 38 additional subtypes. (Swerdlow, et al (eds) WHO Classification Book) As mentioned, over 90% of NHL cases are derived from B-cells. Diffuse large B-cell lymphoma (DLBCL) is the most common type of NHL, representing approximately 30% of all B-cell cases. DLBCL is more common in older individuals, usually becoming apparent in their 60s, but may occur at any age. It is slightly more common in men than women. There are also a number of subtypes of DLBCL, with DLBCL, not otherwise specified, being the most common. DLBCL is a neoplasm of mature B-cells (as opposed to immature B cells of lymphoblastic leukemia), which makes it a chronic disease. Despite the chronic nature of the disease, it is generally more aggressive, if untreated, than most of the lymphomas of small B-cells. DLBCL may also evolve or transform from a more indolent small B-cell lymphoma which may not be apparent at the time of diagnosis. Untreated, DLBCL will spread to lymph nodes and organs throughout the body over months to years and ultimately kill a patient. With current therapy, however, the majority of patients with DLBCL are cured, and the survival of such patients will likely continue to improve as new therapies become available.

7. In most cases, the cause of non-Hodgkin lymphoma (NHL) is unknown (WHO classification book). Although certain risk factors for NHL have been identified, with few exceptions, for an individual patient there is no accepted scientific test, technique or method for determining what caused or contributed to his or her NHL.

8. The best documented cause of NHL is a history of immunodeficiency which may be related to immunosuppression following organ transplantation or related to viral infection. Antigenic stimulation related to specific infections are also associated with an increased risk of NHL even in the absence of immunodeficiency. Infections implicated to increase the risk for NHL include, but are not limited to, human immunodeficiency virus (HIV), Epstein-Barr virus (EBV), hepatitis B virus (HBV), hepatitis C virus (HCV) and H. pylori.
9. HCV infection is well documented in the medical literature to be associated with an increased risk for development of liver cirrhosis, hepatocellular carcinoma and NHL, particularly diffuse large B-cell lymphoma (DLBCL) and splenic marginal zone lymphoma. Maso et al, 2006; Giordano et al, 2007; de Sanjose et al, 2008; Mahale et al, 2017. IARC has concluded that “chronic infection with HCV causes ... non-Hodgkin lymphoma. Chronic infection with HCV is carcinogenic to humans” (Group 1). IARC Monograph 100B (2012). While elimination of measurable HCV using antiviral therapy reduces the risk of development of NHL, there are reports of several cases of NHL arising in this setting, suggesting that such patients remain at risk for development of NHL. (Andrade XA et al, 2018; Lin RJ, et al, 2016)

10. While the mechanism of action is still being investigated, it is known that patients with HCV infection have chronic antigenetic stimulation. This constant stimulation of B-cells, over years, appears to increase the risk for genetic changes in the B-cells that may eventually lead to development of NHL. A similar chronic antigenic response in the liver frequently results in liver disease, including cirrhosis and hepatocellular carcinoma. Other possible mechanisms for HCV to result in lymphoma include the virus actually infecting the B-cells and disrupting the normal cellular function to promote development of cancer, or transient infection of the cells by the virus that causes mutations of specific genes before the virus is expelled from the cell. (Peveling-Oberhag et al, 2013)

11. HBV infection is also documented in the medical literature to be associated with an increased risk for NHL, particularly diffuse large B-cell lymphoma (DLBCL). This association occurs in patients that are Hepatitis B surface antigen positive or that are surface antigen negative, but HBV DNA positive (Dalia et al, 2013; Marcucci et al, 2006; Marcucci et al, 2012; Taborelli et al, 2016; Wang et al, 2007; Wang et al, 2018). These studies did not require the presence of active or symptomatic infection.

12. Other risk factors for NHL are reported and include, but are not limited to, tobacco use, elevated body mass or abdominal girth, and possible dietary factors that include dairy product, red meat and processed meat ingestion.

13. The diagnosis of NHL is made by a pathologist after review of a tissue biopsy, usually a lymph node biopsy. The tissue is processed and glass slides are prepared to review under the microscope. The pathologist reviews the clinical information provided with the specimen, including the age, sex of the patient, relevant medical history and the site of the biopsy prior to reviewing the glass slides under the microscope. NHL distorts the appearance of the tissue under the microscope, resulting in a pattern that is abnormal compared to a normal lymph node slide. The pathologist reviews the pattern of the cells on the slide as well as the size of the cells and the appearance of the cells. If the appearance is abnormal or suspicious, the pathologist then routinely performs special stains to prove whether the cells are B-cells or T-cells as well as other markers that may be useful for the diagnosis and classification of the NHL and to exclude other disorders, if indicated. In rare and difficulty cases, genetic or molecular genetic testing may be performed to assist in the diagnosis, but such tests are not necessary in most cases (with the exception of DLBCL mentioned below).

14. If the studies reveal NHL, the case is classified according to the World Health Organization classification of tumors of hematopoietic and lymphoid tissues. With the exception
of follicular lymphomas, NHL is not specifically graded, but the NHL classification determines whether a case is considered more indolent or more aggressive. For DLBCL, additional prognostic studies, including stains for CD10, BCL6 and MUM1 and fluorescence in situ hybridization (FISH) testing for translocations involving the MYC, BCL2 and BCL6 genes are performed to determine prognosis. In contrast to grading, staging is a clinical activity based on the physical location of the tumor within the body with localized disease being stage 1 and disease spread throughout the body and involving non lymph node organs or the bone marrow as stage 4.

15. On 12/26/2014 (at age 66), Mr. Hardeman presented with swollen lymph nodes in his neck as well as an upper respiratory infection. His lymph node enlargement persisted and he underwent a fine needle aspirate on 1/28/2015 and a diagnostic biopsy on 2/6/2015. Medical records indicate: obesity (BMI = 31 at diagnosis); hypertension; history of alcohol use; past history of smoking cigarettes (stopped around 1980); history of IV drug abuse; cirrhosis; chronic viral hepatitis C contracted in the 1960s and treated with INF therapy in 2005; exposure to hepatitis B; eczema; basal cell carcinoma 2001; subsequent development of melanoma in situ in 2018; glaucoma; and sciatica. Mr. Hardeman reports a brother with skin cancer.

16. I have reviewed the fine needle aspiration slides of the neck lymph node (SRON15-116) which shows an abnormal cell population with necrosis. Flow cytometry immunophenotyping, which would be necessary to further characterize this cell population as lymphoma was not performed. I agree with the interpretation of necrotic tumor. I have also reviewed the bone marrow aspirate, clot section and biopsy (SROS15-2923) which shows normal appearing bone marrow with a few small lymphoid aggregates, but no evidence of involvement by malignant lymphoma. I have reviewed slides labeled SROS15-2109, but none contain tissue. These are labeled as recuts and do not appear to represent the original diagnostic material; therefore, I am currently unable to render an interpretation of this specimen at this time. The fine needle aspirate on 1/28/2015 showed an “extensively necrotic neoplasm,” but due to “tumor necrosis” and “presence of air drying artifact” further evaluation was recommended.

17. A CT scan on 2/3/2015 was suspicious for malignancy.

18. A core biopsy on 2/6/2015 of the lymph nodes in neck found “overall morphologic and immunophenotypic findings consistent with diffuse large B-cell lymphoma.” The pathology report also noted: “large atypical cells are CD20 and PAX5 positive with additional positivity for Bc12. CD3, CD5, Bcl1, CD10, TdT, CD30, Pan-Cytokeratin, S100, and EBER are negative. The Ki67 proliferation rate is approximately 80% of large cells. The bel6 and MUM-1 positivity is consistent with non-germinal center B-cell type.” FISH test was “positive for BCL6 (3q27) rearrangement in 29% (29/100) of cells and a deletion of BCL2 at 18q21 in 32% (32/100) of cells.” In situ hybridization studies for Kappa and Lambda immunoglobulin light chains were positive for Kappa, supporting a clonal B-cell neoplasm.

19. Bone marrow biopsy performed on 2/23/2015 was negative for involvement by lymphoma.

20. He was treated with chemotherapy (R-CHOP (5 agents), 6 treatments), which he tolerated well and currently has no evidence of disease.
21. His treating doctor reports he is in remission after chemotherapy and the last CT scan of 6/2018 shows no evidence of disease.

22. It is my opinion to a reasonable degree of scientific and medical certainty that Mr. Hardeman’s DLBCL demonstrates no unusual features to suggest a specific cause and is similar to most other cases of DLBCL, not otherwise specified. Plaintiffs’ experts Nabhan, Shustov and Weisenberger each acknowledge the idiopathic nature of NHL and DLBCL, yet they fail to set forth any methodology that is accepted in the field of medicine or utilized in the peer-reviewed medical literature that allows them to rule out idiopathic causes of Mr. Hardeman’s NHL.

23. Mr. Hardeman’s hepatitis C infection appears to date back to the 1960s with the effects of immune stimulation for the approximately 40 years prior to treatment. While elimination of measurable HCV using antiviral therapy reduces the risk of development of NHL, there are reports of several cases of NHL arising in this setting, suggesting that such patients remain at risk for development of NHL.(Andrade XA et al, 2018; Lin RJ, et al, 2016). After successful antiviral therapy for HCV, patients remain at risk for developing hepatocellular carcinoma, the most frequent cancer associated with HCV infection. (Aleman S et al, 2013). Mr. Hardeman had a very long period of exposure to HCV with apparent liver damage, and therefore, based on the potential of HCV to cause mutations over his many years of exposure, Mr. Hardeman remained at risk for development of hepatocellular carcinoma and NHL even after his successful treatment of the virus.

24. Mr. Hardeman also had evidence of a prior HBV infection. HBV infection is documented in the medical literature to be associated with an increased risk for NHL, particularly diffuse large B-cell lymphoma (DLBCL). This association occurs in patients that are Hepatitis B surface antigen positive or that are surface antigen negative, but HBV DNA positive (Dalia et al, 2013; Marcucci et al, 2006; Marcucci et al, 2012; Taborelli et al, 2016; Wang et al, 2007; Wang et al, 2018). These studies did not require the presence of active or symptomatic infection and the absence of active infection at the time of Mr. Hardeman’s diagnosis of DLBCL does not exclude the virus’ role in the cause of his lymphoma as suggested by Dr. Weisenberger.

25. Mr. Hardeman had additional risk factors for the development of NHL, and particularly DLBCL, including an elevated body mass index, male gender, age and white ethnicity. There is no indication that Roundup played any role in the development of his NHL, and there are no pathological features to suggest a cause of his lymphoma. The type of tumor that Mr. Hardeman was diagnosed with develops in patients who have not been exposed to Roundup, and there is nothing unusual or unique about his DLBCL pathology or presentation that distinguishes Mr. Hardeman’s DLBCL from patients that have not been exposed to Roundup.

26. Plaintiffs experts inappropriately dismiss or disregard several potential contributors to Mr. Hardeman’s lymphoma and provide no reliable or medically accepted basis for how they rule out these various factors. Likewise, they can point to no reliable or medically accepted method, test or protocol that enables them to arrive at Roundup as a cause or contributor to Mr. Hardeman’s cancer.
27. I reserve right to add/amend opinions if new information or records become available, and to respond to plaintiffs' experts, and to use graphics and demonstratives to explain and illustrate material discussed in the report. I have attached some images of Mr. Hardeman’s pathology to this report as Exhibit E.

Dated: 11/25, 2018

Daniel A. Arber, M.D.