IND 71634
BLA 125388

WRITTEN REQUEST

Seattle Genetics, Inc.
Attention: Lauren Cutler
Director, Regulatory Affairs
21823 30th Drive SE
Bothell, WA 98021

Dear Ms. Cutler:

Reference is made to your February 26, 2021, Proposed Pediatric Study Request for brentuximab vedotin.

These studies investigate the potential use of brentuximab vedotin in the treatment of pediatric patients with previously untreated and relapsed or refractory classical Hodgkin lymphoma (cHL) and systemic anaplastic large cell lymphoma (sALCL).

BACKGROUND:

ADCETRIS® (brentuximab vedotin; BV), a CD30-directed antibody-drug conjugate, is approved in adult patients with Hodgkin lymphoma (HL; Stage III and IV previously untreated and relapsed or refractory [r/r]) and peripheral T-cell lymphoma (PTCL; previously untreated CD30 expressing and r/r systemic anaplastic large cell lymphoma [sALCL]), and primary cutaneous ALCL (pcALCL) and CD30-expressing mycosis fungoides (MF) (who have received prior systemic therapy).

Hodgkin lymphoma and sALCL are rare pediatric hematologic malignancies. Hodgkin lymphoma accounts for about 6% of childhood cancers and sALCL accounts for approximately 10% to 15% of non-Hodgkin lymphoma (NHL) pediatric malignancies[1]. Pediatric HL is among the most curable forms of cancer with 5-year survival rates >90%[2]; however, multi-agent regimens confer a significant morbidity and relapse incidence has been reported to be 15% after 30 years from diagnosis[3]. Similarly, while the standard treatment for childhood sALCL often leads to favorable outcomes, despite having effective therapies for high risk disease, 20-30% of patients eventually relapse[4].

The Food and Drug Administration (FDA) is not requesting studies for HL and sALCL in pediatric patients <5 years of age, including neonates, because of the low incidence of these malignancies in this age group. In addition, studies in patients with pcALCL and CD30-expressing MF are not requested due to the rarity of these diagnoses in the pediatric population.

Representation of Ethnic and Racial Minorities: The studies must take into account adequate (e.g., proportionate to disease population) representation of children of ethnic and racial minorities. If you are not able to enroll an adequate number of these patients, provide a description of your efforts to do so and an explanation for why they were unsuccessful.

To obtain needed pediatric information on brentuximab vedotin, the Food and Drug Administration (FDA) is hereby making a formal Written Request, pursuant to Section 505A of the Federal Food, Drug, and Cosmetic Act (the Act), as amended by the Food and Drug Administration Amendments Act of 2007, that you submit information from the studies described below.

- *Nonclinical study(ies)*:

  Based on review of the available nonclinical toxicology, no additional animal studies are required at this time to support the clinical studies described in this Written Request.

- *Clinical studies:*

Study 1 (C25002)

A Phase 1/2, open-label, single-agent, dose-escalation, global, multicenter study of brentuximab vedotin in pediatric patients with relapsed or refractory (r/r) cHL or r/r sALCL designed to assess safety, tolerability, pharmacokinetics (PK), and antitumor activity. The study was conducted in two phases: a randomized dose-finding phase, followed by safety and efficacy at the recommended Phase 2 dose (RP2D; 1.8 mg/kg on Day 1 of each 21-day cycle).

Study 2 (AHOD1221)

A Phase 1/2, open-label, nonrandomized study designed to identify the optimal dose of brentuximab vedotin for use in combination with gemcitabine and characterize the efficacy and safety of the brentuximab vedotin + gemcitabine combination in pediatric and young adult patients with r/r HL. The study was conducted in two phases: RP2D finding phase, followed by safety and efficacy at the RP2D (1.8 mg/kg on Day 1 of each 21-day cycle).

Study 3 (ANHL12P1)

A Phase 2 randomized study designed to evaluate the treatment of pediatric subjects with previously untreated sALCL using brentuximab vedotin or crizotinib in combination with chemotherapy, compared to historical data from the best treatment arm in Protocol ALCL99 (NCT00006455). Subjects are treated with brentuximab

vedotin (1.8 mg/kg on Day 1 of each 21-day cycle) or crizotinib in combination with chemotherapy over 6 cycles.

Study 4 (HLHR13)

A Phase 2, single-arm study designed to evaluate the safety of AEPA/CAPDac (ADCETRIS [A], etoposide [E], prednisone [P], and doxorubicin [A] / cyclophosphamide [C], ADCETRIS [A], prednisone [P], and dacarbazine [Dac]) as well as the efficacy (early complete response) after 2 cycles of AEPA chemotherapy in high risk subjects with cHL.

Study 5 (AHOD1331)

A Phase 3, randomized study designed to evaluate the efficacy of five 21-day cycles of brentuximab vedotin (1.8 mg/kg) in combination with doxorubicin, vincristine, etoposide, prednisone, and cyclophosphamide (BV-AVEPC) as compared to five 21-day cycles of doxorubicin, bleomycin, vincristine, etoposide, prednisone, and cyclophosphamide (ABVE-PC) in pediatric subjects with high-risk cHL.

- *Study Objectives:*

Study 1 Primary Objectives

- **Phase 1:**
  - To assess the safety profile and determine the pediatric maximum tolerated dose and/or RP2D of brentuximab vedotin.
  - To assess the PK of brentuximab vedotin.
- **Phase 2**
  - To determine the best overall response rate (complete remission [CR], partial remission [PR]) with brentuximab vedotin at the RP2D.

Study 1 Secondary Objectives

- **Phase 1:**
  - To determine the immunogenicity of brentuximab vedotin.
  - To determine best overall response rate (CR, PR) and duration of response with brentuximab vedotin.
- **Phase 2**
  - To determine the time to response and duration of response with brentuximab vedotin.

- To assess the PK and safety profile of brentuximab vedotin.
- To determine the immunogenicity of brentuximab vedotin.

Study 2 Primary Objectives

- To estimate the maximum tolerated dose (MTD) and/or RP2D of brentuximab vedotin in combination with gemcitabine administered every three weeks to children with relapsed or primary refractory Hodgkin lymphoma (HL).
- To define and describe the toxicities of brentuximab vedotin in combination with gemcitabine administered on this schedule.
- To determine the CR rate after treatment with four cycles of gemcitabine with brentuximab vedotin among patients with relapsed or refractory HL.

Study 2 Secondary Objective

- To describe the overall response rate (ORR) after 4 cycles of therapy among patients with relapsed or refractory HL.

Study 3 Primary Objectives

- To determine the tolerability of brentuximab vedotin given in combination with standard chemotherapy (ALCL99).
- To estimate the Event Free Survival (EFS) of the brentuximab vedotin arm and contrast to historical control data.

Study 4 Primary Objective

- To evaluate the safety of Adcetris®, Etoposide, Prednisone, Adriamycin/Cyclophosphamide, Adcertris®, Prednisone, Dacarbazine (AEPA/CAPDAC), as well as the efficacy (early complete response) after 2 cycles of AEPA chemotherapy in high risk patients with Hodgkin lymphoma (HL).

Study 4 Secondary Objectives

- To evaluate the safety of brentuximab vedotin in the AEPA/CAPDac regimen in children with high risk HL.
- To describe pharmacokinetics of brentuximab vedotin when used as part of AEPA/CAPDac for pediatric HL patients (exploratory).

Study 5 Primary Objective

- To assess the EFS of a novel regimen incorporating brentuximab vedotin in the chemotherapy backbone of doxorubicin (Adriamycin), vincristine,

etoposide, prednisone and cyclophosphamide (Bv-AVEPC) in newly diagnosed high-risk cHL compared to those treated with ABVE-PC.

Study 5 Secondary Objectives

- To determine whether children/young adults with high-risk cHL treated with Bv-AVEPC have a higher rate of early response (determined by FDG-PET) and a reduction in response-directed radiation therapy (RT) compared to those treated with ABVE-PC.
- To compare safety, including the rate of neuropathy (>Grade 3), among patients treated on the Bv-AVEPC (experimental arm) to patients treated on the ABVE-PC (standard arm).
- To characterize the pharmacokinetics of brentuximab vedotin in children (exploratory)

- *Patients to be studied:*
    - *Age group in which studies will be performed:*
        - **Study 1:** 2 to ≤18 years (5 to ≤18 for HL)
        - **Study 2:** >12 months and ≤30 years of age
        - **Study 3 :** <22 years
        - **Study 4 :** ≤18 years
        - **Study 5 :** ≥2 and <22 years of age
    - *Number of patients to be studied*
        - **Study 1:** A total of 36 subjects.
            - At least 12 patients less than 12 years of age
            - At least 22 patients 12 years to less than 18 years of age
        - **Study 2:** A total of 46 subjects.
            - At least 3 patients less than 12 years of age
            - At least 24 patients 12 years to less than 18 years of age
        - **Study 3:** A total of 63 subjects.
            - At least 13 patients less than 6 years of age

- At least 19 patients 6 years to less than 12 years of age
- At least 31 patients 12 years to less than 18 years of age

- **Study 4:** A total of 77 subjects. At least 12 patients less than 12 years of age
  - At least 49 patients 12 years to less than 18 years of age
- **Study 5:** A total of 600 subjects.
  - At least 5 patients less than 6 years of age
  - At least 47 patients 6 years to less than 12 years of age
  - At least 220 patients 12 years to less than 18 years of age

- *Study Endpoints:*
  - *Pharmacokinetic Endpoints*
    - **Study 1:** Pharmacokinetic concentration-time profile data of brentuximab vedotin including ADC and MMAE will be summarized. Key Immunogenicity including antitherapeutic antibody (ATA) titer and neutralizing ATA (nATA) assessments
    - **Study 4:** PK and immunogenicity summary statistics
    - **Study 5:** Pharmacokinetic concentration time-profile data of brentuximab vedotin ADC and MMAE. Immunogenicity including ATA assessment.
  - *Efficacy Endpoints:*
    - **Study 1:**
      - Best overall response rate (CR, PR) as determined by independent review facility (IRF) according to International Working Group (IWG) revised response criteria
      - Time to response
      - Duration of response
    - **Study 2:**
      - CR rate
      - ORR

- **Study 3:**
  - EFS
- **Study 4:**
  - CR rate after AEPA
  - EFS
- **Study 5:**
  - EFS
  - Proportion of patients with early response, early response is defined as after 2 cycles of therapy
  - Proportion of patients needing response-directed radiotherapy (RT)

- *Safety Endpoints*
  - **Study 1:** Adverse Events (AEs), Serious Adverse Events (SAEs), assessments of clinical laboratory values, and vital signs measurements
  - **Study 2:** Descriptive summary of all toxicities; individual toxicity counts and incidence rates
  - **Study 3:** Type, incidence, and severity of AEs
  - **Study 4:** Type, incidence, and severity of AEs
  - **Study 5:** Type, incidence, and severity of AEs.

- *Known Drug Safety concerns and monitoring:* Across six adult approved hematological indications in the USPI, the most common adverse reactions (≥ 20% in any clinical study) were peripheral neuropathy, fatigue, nausea, diarrhea, neutropenia, upper respiratory tract infection, pyrexia, constipation, vomiting, alopecia, decreased weight, abdominal pain, anemia, stomatitis, lymphopenia, and mucositis. The warnings and precautions also provide information on case reports and monitoring/management for peripheral neuropathy, anaphylaxis and infusion reactions, hematologic toxicities, serious infections and opportunistic infections, tumor lysis syndrome, hepatotoxicity, progressive multifocal leukoencephalopathy, pulmonary toxicity, serious dermatologic reactions, gastrointestinal complications, hyperglycemia, and embryo-fetal toxicity.

  ADCETRIS can cause fetal harm based on the findings from animal studies and the drug's mechanism of action (clinical pharmacology Section 12.1 of USPI). The available data from case reports on ADCETRIS use in pregnant women are insufficient to inform a drug-associated risk of adverse developmental outcomes. Females of reproductive potential (and males with female partners of

reproductive potential) are advised of the potential risk to a fetus combined with guidance to avoid pregnancy (contraceptive guidance) during ADCETRIS treatment and for at least 6 months after the final dose of ADCETRIS.

The following information pertains to all clinical studies in the Written Request.

- *Extraordinary results:* In the course of conducting these studies, you may discover evidence to indicate that there are unexpected safety concerns, unexpected findings of benefit in a smaller sample size, or other unexpected results. In the event of such findings, there may be a need to deviate from the requirements of this Written Request. If you believe this is the case, you must contact the Agency to seek an amendment. It is solely within the Agency's discretion to decide whether it is appropriate to issue an amendment.

- *Drug information:*
  - *Dosage form:* Sterile, white to off-white lyophilized, preservative-free cake or powder in a single-dose vial for reconstitution

  - *Route of administration:* Intravenous

  - *Regimen (Study 1):* In phase 1, brentuximab vedotin will be administered intravenously on day 1 of each 21-day cycle starting at a dose of 1.4 mg/kg and escalated using a 3+3 design to a maximum dose of 1.8 mg/kg. The recommended phase 2 dose (RP2D) will be administered during phase 2. The dose in patients <18 years will be based on PK and safety analysis of the studies in this request.

  - *Regimen (Study 2):* In phase 1, brentuximab vedotin will be administered intravenously on day 1 of each 21-day cycle starting at 1.4mg/kg and escalated using a 3+3 design to a maximum dose of 1.8 mg/kg in combination with gemcitabine. The recommended phase 2 dose (RP2D) of brentuximab vedotin will be administered during phase 2 in combination with gemcitabine.

  - *Regimen (Study 3):* Brentuximab vedotin will be administered intravenously on day 1 of each 21-day cycle starting at 1.8 mg/kg in combination with chemotherapy.

  - *Regimen (Study 4):* In the first two cycles, brentuximab vedotin 1.2 mg/kg will be administered intravenously on Days 1, 8 and 15 of each 28-day cycle in combination with AEPA. In the subsequent 4 cycles, brentuximab vedotin 1.2 mg/kg will be administered intravenously on Days 1, 8 of each 28-day cycle in combination with CAPDac.

- *Regimen (Study 5):* Brentuximab vedotin 1.8 mg/kg will be administered intravenously on day 1 of each 21-day cycle in combination with AVEPC.

Development of an additional pediatric formulation is not necessary as the current parenteral formulation is appropriate for pediatric use.

- *Statistical information, including power of study(ies) and statistical assessments:*
  - **Study 1:**
    - *Safety:* Safety will be evaluated by the incidence of AEs, severity and type of AEs, and by changes from baseline in the patient's vital signs, neurotoxicity assessment, ECGs, and clinical laboratory results using the safety population.

    - *PK:* Descriptive statistics (eg, number of subjects, arithmetic mean, geometric mean, standard deviation, median, percentage of coefficient of variation, minimum, and maximum) will be used to summarize PK parameters of brentuximab vedotin, total therapeutic antibody, and MMAE for each cohort. Immunogenicity parameters (ATA titer and neutralizing ATA titer) will be summarized using descriptive statistics. Individual and mean plasma concentration data will be plotted over time. Descriptive statistics will be presented for serum PK parameters.

      Efficacy: The best ORR, CR rate, PR rate, time to response, and duration of response (DOR) will be analyzed. The 2-sided 95% exact binomial confidence interval on the percentage of patients falling into each response category will be established.
  - **Study 2:**
    - *Safety:* Type, incidence, and severity of adverse events will be summarized for patients receiving study treatment. Summaries will include patients in Part A and B of the study, with patients presented by dose level of brentuximab vedotin administered (1.4 mg/kg or 1.8 mg/kg).

    - *Efficacy:* The complete response rate for patients receiving 4 cycles of gemcitabine and brentuximab vedotin will be presented with the corresponding 95% confidence interval. Patients will be presented according to the brentuximab vedotin dose level received (1.4 mg/kg or 1.8 mg/kg). Similar summaries will be presented for ORR.

  - **Study 3:**

- *Safety:* Type, incidence, and severity of adverse events will be summarized, including certain Grade 3+ non-hematologic toxicities for each regimen.

- *Efficacy:* The EFS for each of the treatment regimens will be summarized using Kaplan-Meier methodology. EFS estimates will be presented by year from randomization, with corresponding 95% confidence intervals. Median EFS will be presented with the corresponding 95% confidence interval (if estimable).

- **Study 4**
  - *Safety:* Summary statistics for incidence and severity will be provided for adverse events, including hematologic, neuropathic and infectious toxicities.

  - *PK:* Descriptive statistics will be used to summarize concentration-time profile data of brentuximab vedotin ADC and MMAE. Key PK parameters to be assessed include CL, AUC, $t_{1/2}$.

  - *Efficacy:* The CR rate after AEPA will be estimated, and the corresponding exact 95% confidence interval will be presented. EFS will be summarized using Kaplan-Meier methodology, with estimated EFS rates and 95% confidence intervals presented for the 2 and 3-year time points.

- **Study 5**
  - *Safety:* Type, incidence, and severity of adverse events will be summarized. The proportion of patients experiencing Grade 3+ peripheral neuropathy (assessed by modified Balis scale) after the first 2 cycles and after all 5 cycles of chemotherapy will be estimated for the Bv-AVEPC arm and for ABVE-PC.

  - *PK:* Descriptive statistics will be used to summarize concentration-time profile data of brentuximab vedotin ADC and MMAE. Key PK parameters to be assessed include CL, AUC, $t_{1/2}$.

  - *Efficacy:* EFS, defined as disease progression or relapse, second malignancy, or death, will be summarized by treatment arm for the intent-to-treat population using Kaplan-Meier methodology. The primary analysis will be based on a 1-sided log rank test comparison of EFS curves between the 2 randomized arms, with alpha adjustment according to the pre-specified interim analyses Estimated EFS rates and corresponding 95% confidence intervals will be presented for the 2- and 3-year timepoints.

Assuming a 3-year EFS of 82% for standard arm, the study will have approximately 86% power for detecting an 8% improvement in 3-year EFS in the Bv-AVEPC arm (3-year EFS of 90% in log rank test when the EFS curves follow a cure model. Power estimation is based on 290 eligible patients per arm and 1-sided log rank test with alpha level of 0.05.

The proportion of patients achieving early response (i.e., with no SRL and no PD at all sites) as well as the difference in proportions will be summarized for the two randomized arms. 95% confidence intervals will be presented for the corresponding estimates. The proportion of patients needing response-directed RT (including PD) will be summarized based on similar methodology.

One interim analysis for EFS will occur after approximately 50% of the expected events.

- *Labeling that may result from the study(ies)*: You must submit proposed pediatric labeling to incorporate the findings of the study(ies). Under section 505A(j) of the Act, regardless of whether the study(ies) demonstrate that brentuximab vedotin is safe and effective, or whether such study results are inconclusive in the studied pediatric population(s) or subpopulation(s), the labeling must include information about the results of the study(ies). Under section 505A(k)(2) of the Act, you must distribute to physicians and other health care providers at least annually (or more frequently if FDA determines that it would be beneficial to the public health), information regarding such labeling changes that are approved as a result of the study(ies).

- *Format and types of reports to be submitted*: You must submit full study reports (which have not been previously submitted to the Agency) that address the issues outlined in this request, with full analysis, assessment, and interpretation. In addition, the reports must include information on the representation of pediatric patients of ethnic and racial minorities. All pediatric patients enrolled in the study(ies) should be categorized using one of the following designations for race: American Indian or Alaska Native, Asian, Black or African American, Native Hawaiian or other Pacific Islander or White. For ethnicity, you should use one of the following designations: Hispanic/Latino or Not Hispanic/Latino. If you choose to use other categories, you should obtain agency agreement.

  Under section 505A(d)(2)(B) of the Act, when you submit the study reports, you must submit all postmarketing adverse event reports regarding this drug that are available to you at that time. All post-market reports that would be reportable under section 21 CFR 314.80 should include adverse events occurring in an adult or a pediatric patient. In general, the format of the post-market adverse event report should follow the model for a periodic safety update report described

in the guidance for industry *E2C Clinical Safety Data Management: Periodic Safety Update Reports for Marketed Drugs* and the guidance addendum.[1] You are encouraged to contact the reviewing Division for further guidance.

Although not currently required, we request that study data be submitted electronically according to the Study Data Tabulation (SDTM) standard published by the Clinical Data Interchange Standards Consortium (CDISC) provided in the document "Study Data Specifications," which is posted on FDA.gov[2] and referenced in the guidance for industry *Providing Regulatory Submissions in Electronic Format - Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications*.

Timeframe for submitting reports of the study(ies): Reports of the above studies must be submitted to the Agency on or before 04/30/2022. Please keep in mind that pediatric exclusivity attaches only to existing patent protection or exclusivity that would otherwise expire nine (9) months or more after pediatric exclusivity is granted, and FDA has 180 days from the date that the study reports are submitted to make a pediatric exclusivity determination. Therefore, to ensure that a particular patent or exclusivity is eligible for pediatric exclusivity to attach, you are advised to submit the reports of the studies at least 15 months (9 months plus 6 months/180 days for determination) before such patent or exclusivity is otherwise due to expire.

- *Response to Written Request:* Under section 505A(d)(2)(A)(i), within 180 days of receipt of this Written Request you must notify the Agency whether or not you agree to the Written Request. If you agree to the request, you must indicate when the pediatric studies will be initiated. If you do not agree to the request, you must indicate why you are declining to conduct the study(ies). If you decline on the grounds that it is not possible to develop the appropriate pediatric formulation, you must submit to us the reasons it cannot be developed.

  Furthermore, if you agree to conduct the study(ies), but have not submitted the study reports on or before the date specified in the Written Request, the Agency may utilize the process discussed in section 505A(n) of the Act.

Submit protocols for the above study(ies) to an investigational new drug application (IND) and clearly mark your submission **"PEDIATRIC PROTOCOL SUBMITTED FOR PEDIATRIC EXCLUSIVITY STUDY"** in large font, bolded type at the beginning of the cover letter of the submission.

[1] We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database https://www.fda.gov/RegulatoryInformation/Guidances/default.htm
[2] https://www.fda.gov/downloads/ForIndustry/DataStandards/StudyDataStandards/UCM312964.pdf

Reports of the study(ies) must be submitted as a new drug application (NDA) or as a supplement to your approved NDA with the proposed labeling changes you believe are warranted based on the data derived from these studies. When submitting the reports, please clearly mark your submission "**SUBMISSION OF PEDIATRIC STUDY REPORTS - PEDIATRIC EXCLUSIVITY DETERMINATION REQUESTED**" in large font, bolded type at the beginning of the cover letter of the submission and include a copy of this letter.

In accordance with section 505A(k)(1) of the FD&C Act, *Dissemination of Pediatric Information*, FDA must make available to the public the medical, statistical, and clinical pharmacology reviews of the pediatric studies conducted in response to this Written Request within 210 days of submission of your study report(s). These reviews will be posted regardless of the following circumstances:

(1) the type of response to the Written Request (i.e. complete or partial response);
(2) the status of the application (i.e. withdrawn after the supplement has been filed or pending);
(3) the action taken (i.e. approval, complete response); or
(4) the exclusivity determination (i.e. granted or denied).

FDA will post the medical, statistical, and clinical pharmacology reviews on the FDA website.[3]

If you wish to discuss any amendments to this Written Request, please submit proposed changes and the reasons for the proposed changes to your application. Submissions of proposed changes to this request should be clearly marked "**PROPOSED CHANGES IN WRITTEN REQUEST FOR PEDIATRIC STUDIES"** in large font, bolded type at the beginning of the cover letter of the submission. You will be notified in writing if any changes to this Written Request are agreed upon by the Agency.

Please note that, if your trial is considered an "applicable clinical trial" under section 402(j)(1)(A)(i) of the PHS Act, you are required to comply with the provisions of section 402(j) of the PHS Act with regard to registration of your trial and submission of trial results. Additional information on submission of such information can be found on the Clinical Trials website.[4]

If you have any questions, call Thomas Iype, Regulatory Project Manager, at 240-402-6861.

[3] https://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/ucm316937.htm
[4] www.ClinicalTrials.gov

Sincerely,

{See appended electronic signature page}

Gregory Reaman, MD
Acting Associate Director, Pediatric Oncology
Office of Oncological Diseases
Center for Drug Evaluation and Research

References

1 Le Deley MC, Reiter A, Williams D, Delsol G, Oschlies I, McCarthy K, Zimmermann M, Brugieres L, European Intergroup for Childhood Non-Hodgkin Lymphoma (2008). Prognostic factors in childhood anaplastic large cell lymphoma: results of a large European intergroup study. Blood 111(3): 1560-6

2 Kelly KM (2015). Hodgkin lymphoma in children and adolescents: improving the therapeutic index. Blood 126(22): 2452-8

3 Castellino SG, AM; Mertens, AC; Leisenring, WM; Tooze, JA; Goodman, P; Stovall, M; Robison, LL; Hudson, MM (2011). Morbidity and mortality in long-term survivors of Hodgkin lymphoma: a report from the Childhood Cancer Survivor Study. Blood 117(6): 1806-1816.

4 Lowe EJ, Gross TG (2013). Anaplastic large cell lymphoma in children and adolescents. Pediatr Hematol Oncol 30(6): 509-19

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

GREGORY H REAMAN
07/12/2021 10:20:51 AM