

18<sup>th</sup> December 2008



**National Institute for  
Health and Clinical Excellence**

MidCity Place  
71 High Holborn  
London  
WC1V 6NA

Dear [REDACTED]

**Single Technology Appraisal – Mifamurtide for the treatment of  
osteosarcoma**

The Evidence Review Group (ERG), SchARR Technology Assessment Group, and the technical team at NICE have had an opportunity to take a look at the information provided by IDM Pharma on 8<sup>th</sup> December 2008 and have some final requests for information.

Both the ERG and the technical team at NICE will be addressing these points in their reports. As there will not be any consultation on the evidence report prior to the Appraisal Committee meeting you may want to respond to our request and provide further discussion from your perspective at this stage.

We request you to provide a written response to this letter to the Institute by **8th January 2009** to [REDACTED]. Two versions of this written response should be submitted; one with academic/commercial in confidence information clearly marked and one from which this information is removed.

Please underline all confidential information, and separately highlight information that is submitted under 'commercial in confidence' in red and all information submitted under 'academic in confidence' in yellow.

If you present data that is not already referenced in the main body of your submission and that data is seen to be academic/commercial in confidence information, please complete the attached checklist for in confidence information.

Yours sincerely

[REDACTED]  
Associate Director - Appraisals  
Centre for Health Technology Evaluation

Encl. checklist for in confidence information

## **Section A. Clarification on effectiveness data**

- A1. *Please clarify your response to A21 (p20 of the IDM Pharma response to clarification) by providing the following data and/or justification in the grey cells of Tables 1a and 1b on pages 4 and 5 below.*
- A2. *Please clarify whether table A21b (p20 of the IDM Pharma response to clarification) refers to overall survival or disease survival. If A21b refers to overall survival, please provide corresponding data for disease free survival or vice versa*
- A3. *Please provide the overall comparison of MEPACT vs. No MEPACT in table A21b (p20 of the IDM Pharma response to clarification) for both overall survival and disease free survival.*
- A4. *The median follow up between the two data sets (2006 and 2007) in Table A21a (p20 of the IDM Pharma response to clarification) appear to be very similar, please clarify if this correct.*
- A5. *The submission by IDM Pharma (p55) also suggests that the median follow up for the 2007 data set was 7.9 years, whereas the median follow-up in the 2007 data set (Table A21a of the IDM Pharma response to clarification) suggests a range from 6.0 to 6.7 years. Please provide further clarification.*
- A6. *Please provide all respective data for the 2003 data set, including Kaplan-Meier curves for the four treatment groups for the 2003 data set, including numbers at risk at each time point.*
- A7. *Please provide Kaplan-Meier curves for the MEPACT and no MEPACT groups for the 2003, 2006 and 2007 data set, including numbers at risk at each time point.*

**Table 1a: Overall survival outcome efficacy data (confirm (all data) and provide data for all cells highlighted in grey)**

| Treatment                        | Median follow up (years) | Numbers followed in each group (n vs. n) | Events in each group (n vs. n) | HR (95% CI; p value)        |
|----------------------------------|--------------------------|--|--------------------------------|-----------------------------|
| <b>2003 data set for OS</b>      |                          |  |                                |                             |
| A (control)                      |                          |  |                                | -                           |
| A+                               |                          |  |                                | -                           |
| B                                |                          |  |                                | -                           |
| B+                               |                          |  |                                | -                           |
| Primary analysis                 |                          |  |                                |                             |
| A/B combined vs. A+/ B+ combined |                          | 340 vs. 338                              | 85 vs. 63                      | 0.68 (0.49,0.95; p=0.0183)  |
| Additional analysis              |                          |  |                                |                             |
| A vs. A+                         | -                        |  |                                |                             |
| A vs. B                          | -                        |  |                                |                             |
| A vs. B+                         | -                        |  |                                |                             |
| B vs. A+                         | -                        |  |                                |                             |
| A+ vs. B+                        | -                        |  |                                |                             |
| B vs. B+                         | -                        |  |                                |                             |
| <b>2006 data set for OS</b>      |                          |  |                                |                             |
| A (control)                      | 5.9                      | 174                                      | 51 (29%)                       | -                           |
| A+                               | 6.2                      | 167                                      | 37 (22%)                       | -                           |
| B                                | 5.9                      | 166                                      | 49 (30%)                       | -                           |
| B+                               | 6.1                      | 171                                      | 36 (21%)                       | -                           |
| Primary analysis                 |                          |  |                                |                             |
| A/B combined vs. A+/ B+ combined |                          | 340 vs. 338                              | 100 vs. 73                     | 0.72 (0.53, 0.98; p=0.0352) |
| Additional analysis              |                          |  |                                |                             |
| A vs. A+                         | -                        | 174 vs. 167                              | 51 vs. 37                      |                             |
| A vs. B                          | -                        | 174 vs. 166                              | 51 vs. 49                      |                             |
| A vs. B+                         | -                        | 174 vs. 171                              | 51 vs. 36                      |                             |
| B vs. A+                         | -                        | 166 vs. 167                              | 49 vs. 37                      |                             |
| A+ vs. B+                        | -                        | 167 vs. 171                              | 37 vs. 36                      |                             |
| B vs. B+                         | -                        | 166 vs. 171                              | 49 vs. 36                      |                             |
| <b>2007 data set for OS</b>      |                          |  |                                |                             |
| A (control)                      | 6.0                      | 174                                      | 51 (29%)                       | -                           |
| A+                               | 6.7                      | 167                                      | 37 (22%)                       | -                           |
| B                                | 6.3                      | 166                                      | 49 (30%)                       | -                           |
| B+                               | 6.2                      | 171                                      | 36 (21%)                       | -                           |
| Primary analysis                 |                          |  |                                |                             |
| A/B combined vs. A+/ B+ combined |                          | 340 vs. 338                              | 100 vs. 73                     | 0.72 (0.53, 0.97; p=0.0313) |
| Additional analysis              |                          |  |                                |                             |
| A vs. A+                         | -                        | 174 vs. 167                              | 51 vs. 37                      |                             |
| A vs. B                          | -                        | 174 vs. 166                              | 51 vs. 49                      |                             |
| A vs. B+                         | -                        | 174 vs. 171                              | 51 vs. 36                      |                             |
| B vs. A+                         | -                        | 166 vs. 167                              | 49 vs. 37                      |                             |
| A+ vs. B+                        | -                        | 167 vs. 171                              | 37 vs. 36                      |                             |
| B vs. B+                         | -                        | 166 vs. 171                              | 49 vs. 36                      |                             |

**Table 1b: Disease free survival outcome efficacy data (confirm (all data) and provide data for all cells highlighted in grey)**

| Treatment                        | Median follow up (years) | Numbers followed in each group (n vs. n) | Events in each group (n vs. n) | HR (95% CI; p value)        |
|----------------------------------|--------------------------|--|--------------------------------|-----------------------------|
| <b>2003 data set for DFS</b>     |                          |  |                                |                             |
| A (control)                      |                          |  |                                | -                           |
| A+                               |                          |  |                                | -                           |
| B                                |                          |  |                                | -                           |
| B+                               |                          |  |                                | -                           |
| Primary analysis                 |                          |  |                                |                             |
| A/B combined vs. A+/ B+ combined |                          | 340 vs.338                               | 126 vs. 102                    | 0.76 (0.58, 0.98; p=0.0245) |
| Additional analysis              |                          |  |                                |                             |
| A vs. A+                         | -                        |  |                                |                             |
| A vs. B                          | -                        |  |                                |                             |
| A vs. B+                         | -                        |  |                                |                             |
| B vs. A+                         | -                        |  |                                |                             |
| A+ vs. B+                        | -                        |  |                                |                             |
| B vs. B+                         | -                        |  |                                |                             |
| <b>2006 data set for DFS</b>     |                          |  |                                |                             |
| A (control)                      | 5.9                      | 174                                      | 62 (36%)                       | -                           |
| A+                               | 6.2                      | 167                                      | 58 (35%)                       | -                           |
| B                                | 5.9                      | 166                                      | 71 (43%)                       | -                           |
| B+                               | 6.1                      | 171                                      | 49 (29%)                       | -                           |
| Primary analysis                 |                          |  |                                |                             |
| A/B combined vs. A+/ B+ combined |                          | 340 vs.338                               | 133 vs. 107                    |                             |
| Additional analysis              |                          |  |                                |                             |
| A vs. A+                         | -                        | 174 vs. 167                              | 62 vs. 58                      |                             |
| A vs. B                          | -                        | 174 vs. 166                              | 62 vs. 71                      |                             |
| A vs. B+                         | -                        | 174 vs. 171                              | 62 vs. 49                      |                             |
| B vs. A+                         | -                        | 166 vs. 167                              | 71 vs. 58                      |                             |
| A+ vs. B+                        | -                        | 167 vs. 171                              | 58 vs. 49                      |                             |
| B vs. B+                         | -                        | 166 vs. 171                              | 71 vs. 49                      |                             |
| <b>2007 data set for DFS</b>     |                          |  |                                |                             |
| A (control)                      | 6.0                      | 174                                      | 62 (36%)                       | -                           |
| A+                               | 6.7                      | 167                                      | 58 (35%)                       | -                           |
| B                                | 6.3                      | 166                                      | 71 (43%)                       | -                           |
| B+                               | 6.2                      | 171                                      | 49 (29%)                       | -                           |
| Primary analysis                 |                          |  |                                |                             |
| A/B combined vs. A+/ B+ combined |                          | 340 vs.338                               | 133 vs. 107                    |                             |
| Additional analysis              |                          |  |                                |                             |
| A vs. A+                         | -                        | 174 vs. 167                              | 62 vs. 58                      |                             |
| A vs. B                          | -                        | 174 vs. 166                              | 62 vs. 71                      |                             |
| A vs. B+                         | -                        | 174 vs. 171                              | 62 vs. 49                      |                             |
| B vs. A+                         | -                        | 166 vs. 167                              | 71 vs. 58                      |                             |
| A+ vs. B+                        | -                        | 167 vs. 171                              | 58 vs. 49                      |                             |
| B vs. B+                         | -                        | 166 vs. 171                              | 71 vs. 49                      |                             |

