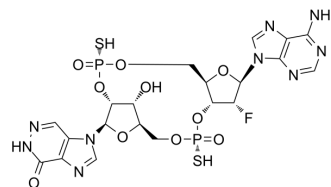


## BI 7446

|                    |  |
|--------------------|--|
| Cat. No.:          | HY-155100  |
| CAS No.:           | 2767011-00-5   |
| Molecular Formula: | C <sub>20</sub> H <sub>22</sub> N <sub>9</sub> O <sub>10</sub> P <sub>2</sub> S <sub>2</sub> |
| Molecular Weight:  | 693.52   |
| Target:            | STING  |
| Pathway:           | Immunology/Inflammation  |
| Storage:           | Please store the product under the recommended conditions in the Certificate of Analysis.    |



### BIOLOGICAL ACTIVITY

|                    |  |               |   |                |              |                  |                              |         |   |               |   |
|--------------------|--|---------------|---|----------------|--------------|------------------|------------------------------|---------|---|---------------|---|
| <b>Description</b> | BI 7446 is a cyclic dinucleotide (CDN)-based potent and selective stimulator of interferon genes (STING) agonist. BI 7446 can activate all five STING variants in cells and induce tumor-specific immune-mediated tumor rejection. BI 7446 can be used for immuno-oncology research <sup>[1]</sup> .   |               |   |                |              |                  |                              |         |   |               |   |
| <b>In Vitro</b>    | <p>BI 7446 (CDN13) (3 μM, 10 μM, 6 h) increases IRF3 and TBK1 phosphorylation in THP1 STING-wild type cells<sup>[1]</sup>. MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p> <p>Western Blot Analysis<sup>[1]</sup></p> <table border="1"> <tr> <td>Cell Line:</td> <td>wild type and STING-knock out THP1 cells</td> </tr> <tr> <td>Concentration:</td> <td>3 μM, 10 μM</td> </tr> <tr> <td>Incubation Time:</td> <td>6 h</td> </tr> <tr> <td>Result:</td> <td>Observed a dose dependent increase of IRF3 and TBK1 phosphorylation in THP1 wild type cells but not in THP1 STING knockout cells.</td> </tr> </table>  | Cell Line:    | wild type and STING-knock out THP1 cells    | Concentration: | 3 μM, 10 μM  | Incubation Time: | 6 h                          | Result: | Observed a dose dependent increase of IRF3 and TBK1 phosphorylation in THP1 wild type cells but not in THP1 STING knockout cells. |               |   |
| Cell Line:         | wild type and STING-knock out THP1 cells   |               |   |                |              |                  |                              |         |   |               |   |
| Concentration:     | 3 μM, 10 μM  |               |   |                |              |                  |                              |         |   |               |   |
| Incubation Time:   | 6 h  |               |   |                |              |                  |                              |         |   |               |   |
| Result:            | Observed a dose dependent increase of IRF3 and TBK1 phosphorylation in THP1 wild type cells but not in THP1 STING knockout cells.  |               |   |                |              |                  |                              |         |   |               |   |
| <b>In Vivo</b>     | <p>BI 7446 (CDN13) (4, 12, 36 μg for intravenous injection, 0-25 h for detection time) has a high plasma clearance and a short elimination half-life in 4T1 BALB/c mouse tumor model<sup>[1]</sup>.</p> <p>BI 7446 (0.25, 1, 4 μg for subcutaneous injection, once weekly) generates tumor regression and a long-term immunologic memory against autologous tumor re-challenge in EMT6 mouse breast cancer model<sup>[1]</sup>.</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p> <table border="1"> <tr> <td>Animal Model:</td> <td>4T1 BALB/c mouse tumor model<sup>[1]</sup></td> </tr> <tr> <td>Dosage:</td> <td>4, 12, 36 μg</td> </tr> <tr> <td>Administration:</td> <td>Intravenous injection (i.v.)</td> </tr> <tr> <td>Result:</td> <td>Observed a high plasma clearance and a short elimination half-life.</td> </tr> </table><br><table border="1"> <tr> <td>Animal Model:</td> <td>EMT6 mouse breast cancer model<sup>[1]</sup></td> </tr> </table> | Animal Model: | 4T1 BALB/c mouse tumor model <sup>[1]</sup> | Dosage:        | 4, 12, 36 μg | Administration:  | Intravenous injection (i.v.) | Result: | Observed a high plasma clearance and a short elimination half-life.   | Animal Model: | EMT6 mouse breast cancer model <sup>[1]</sup> |
| Animal Model:      | 4T1 BALB/c mouse tumor model <sup>[1]</sup>  |               |   |                |              |                  |                              |         |   |               |   |
| Dosage:            | 4, 12, 36 μg   |               |   |                |              |                  |                              |         |   |               |   |
| Administration:    | Intravenous injection (i.v.)   |               |   |                |              |                  |                              |         |   |               |   |
| Result:            | Observed a high plasma clearance and a short elimination half-life.  |               |   |                |              |                  |                              |         |   |               |   |
| Animal Model:      | EMT6 mouse breast cancer model <sup>[1]</sup>  |               |   |                |              |                  |                              |         |   |               |   |

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|                 |   |
|-----------------|---|
| Dosage:         | 0.25, 1, 4 µg   |
| Administration: | Subcutaneous injection (s.c.)   |
| Result:         | Observed dose-dependent tumor regression even at the lowest tested dose.<br>Impaired the growth of the EMT6 tumors. |

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## REFERENCES

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[1]. Kuttruff CA, et al. Discovery of BI 7446: A Potent Cyclic Dinucleotide STING Agonist with Broad-Spectrum Variant Activity for the Treatment of Cancer. J Med Chem. 2023 Jul 27;66(14):9376-9400.

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**Caution: Product has not been fully validated for medical applications. For research use only.**

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