

## Product Datasheet

### AT-9283 (orb1223726)

**Catalog Number** orb1223726

**Category** Small Molecules

**Description** A multi-targeted kinase inhibitor with potent activity against Aurora A, Aurora B, JAK2, JAK3, and ABL (T315I) with IC50 of 3, 3, 1.2, 1.1, and 4 nM, respectively; also inhibits GSK-3 $\beta$ , FGFR2, VEGFR3, Mer, etc. (IC50=1-10 nM); potently inhibits proliferation and Jak2-related signalling in Jak2-dependent cell lines, demonstrates significant therapeutic potential in vivo in an ETV6-JAK2 (TEL-JAK2) murine leukaemia model. Blood Cancer Phase 2 Clinical(In Vitro):AT9283 leads to a clear polyploid phenotype by inhibiting the activity of Aurora B kinase in HCT116 cells with IC50 of 30 nM. Furthermore, AT9283 also produces the potent inhibition on HCT116 colony formation.AT9283 induces apoptosis in a dose and time dependent manner and inhibits cell proliferation with an IC50 < 1  $\mu$ M in B-NHL cell lines.AT9283 inhibits growth, induces dose dependent cytotoxicity, and inhibits STAT3 signaling pathway in MM cell lines. T9283 inhibits phospho Histone H3 and phospho Aurora A at Thr 288. AT9283 increases G2/M phase and induces apoptosis of MM cells in a time-dependent manner.\n(In Vivo):In HCT116 human colon carcinoma xenograft bearing mice, AT9283 treatment (15 mg/kg and 20 mg/kg) for 16 days results in a significant tumor growth inhibition of 67% and 76%, respectively. In addition, AT9283 also exhibits a significantly longer half-life in tumors (2.5 hours) compared with plasma (0.5 hour) and modest oral bioavailability in mice.AT9283 (15 mg/kg) and docetaxel (10 mg/kg) alone has modest anti-tumor activity. T9283 at 20 mg/kg and AT9283 (15 or 20 mg/kg) plus docetaxel (10 mg/kg) demonstrate a statistically significant tumor growth inhibition and enhance survival in mouse xenograft model of mantle cell lymphoma.AT9283 (45 mg/kg, i.p.) inhibits tumor growth in mice. Two cycles of AT9283 45 mg/kg 14 hours after drug administration confirm decreased expression of phospho-Histone H3 and Aurora B in treated animals.

**Target** Aurora Kinase

**Purity** >98% (HPLC)

**MW** 381.4316

#### **Biorbyt Ltd.**

7 Signet Court, Swann Road  
Cambridge  
CB5 8LA  
United Kingdom

Email: [info@biorbyt.com](mailto:info@biorbyt.com), [support@biorbyt.com](mailto:support@biorbyt.com)  
Phone: [+44 \(0\)1223 859353](tel:+44(0)1223859353) | Fax: [+1 \(415\) 651-8558](tel:+1(415)651-8558)

#### **Biorbyt LLC**

68 TW Alexander Drive  
Research Triangle Park  
Durham  
NC 27713  
United States

Email: [info@biorbyt.com](mailto:info@biorbyt.com), [support@biorbyt.com](mailto:support@biorbyt.com)  
Phone: [+1 \(415\) 906-5211](tel:+1(415)906-5211) | Fax: [+1 \(415\) 651-8558](tel:+1(415)651-8558)

<b>Target Areas</b>	Abl1(T315I) AuroraA AuroraB JAK2 JAK3
<b>Solubility (25°C)</b>	10 mM in DMSO
<b>CAS Number</b>	896466-04-9
<b>Formula</b>	C <sub>19</sub> H <sub>23</sub> N <sub>7</sub> O <sub>2</sub>
<b>SMILES</b>	<chem>C1CC1NC(=O)NC\2=CN/C2=C\3/N=C4C=CC(=CC4=N3)CN5CCOCC5</chem>
<b>Chemical Name</b>	Urea, N-cyclopropyl-N'-[3-[6-(4-morpholinylmethyl)-1H-benzimidazol-2-yl]-1H-pyrazol-4-yl]-
<b>Storage</b>	Storage temperature: -20°C. Stability: ≥ 2 years
<b>Note</b>	For research use only
<b>Expiration Date</b>	12 months from date of receipt.

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7 Signet Court, Swann Road  
Cambridge  
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United Kingdom

Email: [info@biorbyt.com](mailto:info@biorbyt.com), [support@biorbyt.com](mailto:support@biorbyt.com)

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Phone: [+1 \(415\) 906-5211](tel:+1(415)906-5211) | Fax: [+1 \(415\) 651-8558](tel:+1(415)651-8558)