## From Nature to Bench to Bedside

History of the Discovery and Development of Taxol and Camptothecin

## **TAXOL Timeline**

1962

Taxus brevitolia collected in Washington state

1966-70

Taxol

isolated

Studies to characterize

1971

Taxol structure reported to J. of taxol structure Am. Chem. Soc.

1979

Unique mechanism of action determined: promoting and stabilizing microtubule assembly ovarian cancer

In 1966 RTI chemists isolated Taxol from the bark of Taxus brevifolia, and

in 1971 Drs. Wall, Wani, and colleagues published its complete structure. Discovery of its unique mode of action by Dr. Susan Horwitz in 1979 catalyzed

taxol's development by NCI. Supplies of the naturally occurring drug limited progress, but response rates in ovarian cancer clinical trials were remarkable.

Bristol-Myers Squibb obtained rights to develop taxol and, in late 1992, FDA

approval was grated for its use in refractory ovarian cancer. In 1993, a semi-

synthetic route for taxol from renewable precursors resolved both supply

1985-86

Phase II clinical trials, activity in 1992

Approved in record time for use against refractory ovarian cancer

1997

Approved for AIDSrelated Kaposi's sarcoma in the US

2002

Historical marker dedicated to commemorate original collection of Taxus bevifolia 40 years earlier

## 1965 1966

Sample assigned to RTI for bioactivity-directed fractionation, based on in pure NCI results of 1964 form

1970 Defining Moments

January

X-ray structure of methyl ester side chain X-ray structure of taxane core Tentative structure of taxol Final structure of taxol

1975-76

and environmental concerns.

Taxol evaluated against a panel of tumor systems 1983-84

Phase 1 Clinical trials

1988-90

Semisynthesis of taxol

1994

Approved for use against breast cancer 1999

Taxol/cisplatin approved in US for non-small-cell lung cancer

2003

RTI's Natural Products Laboratory bestowed National Historic Chemical Landmark