NCCN Request for Proposals (RFP): Phase I/II Clinical Trials of Zipalertinib (CLN 081/TAS 6417) for Non-Small Cell Lung Cancers with Epidermal Growth Factor Receptor (*EGFR)* Exon 20 Insertions or Uncommon/Compound Mutations

Date Issued: October 30, 2024
Date Re-Issued: January 21, 2025

1.0 Purpose

The National Comprehensive Cancer Network (NCCN) and Taiho Oncology, Inc. are collaborating to offer a new grant opportunity seeking proposals for investigator-initiated research with Zipalertinib. NCCN has received a research grant from Taiho (hereafter, "Grantor") to support NCCN Member Institution faculty for the performance of clinical studies to further evaluate the effectiveness of zipalertinib in the treatment of Non-Small Cell Lung Cancers (NSCLC) with *EGFR* mutations including Exon 20 insertion (Ex20ins) mutations and other uncommon mutations. NCCN will serve as the funding organization. Grants are available only to investigators from NCCN Member Institutions.

2.0 Organization Information

National Comprehensive Cancer Network

The National Comprehensive Cancer Network® (NCCN®) is a not-for-profit alliance of 33 leading cancer centers devoted to patient care, research, and education. NCCN is dedicated to improving and facilitating quality, effective, efficient, and equitable cancer care so patients can live better lives. Through the leadership and expertise of clinical professionals at NCCN Member Institutions, NCCN develops resources that present valuable information to the numerous stakeholders in the health care delivery system. By defining and advancing high-quality cancer care, NCCN promotes the importance of continuous quality improvement and recognizes the significance of creating clinical practice guidelines appropriate for use by patients, clinicians, and other health care decision-makers around the world.

Grantor

The Grantor is Taiho Oncology, Inc. located at 101 Carnegie Center, Suite 101, Princeton, NJ 08540.

3.0 Background

NCCN received a grant from the Grantor for the design and performance of clinical trials using zipalertinib (formerly CLN-081/TAS6417) to treat patients with *EGFR*-mutated NSCLC.

Mechanism of Action

Zipalertinib is a novel, oral tyrosine kinase inhibitor (TKI) with high selectivity for mutated *EGFR*. Its unique pyrrolopyrimidine scaffold forms a covalent bond with C797, which exhibits slow-dissociation kinetics and irreversible inhibition of receptor phosphorylation.

Preclinical Data
While zipalertinib is being developed particularly to treat those with *EGFR* Ex20ins mutations, the drug also shows activity against other uncommon *EGFR* mutations (*e.g.*, G719X, L861Q, S768I, compound mutations) as well as common *EGFR* mutations (*e.g.*, Exon 19 del, L858R). In vitro competition assays across several common *EGFR* Ex20ins consistently demonstrate IC_{50} of 175 nM or less with high selectivity ratios (WT *EGFR* IC_{50}/mutant *EGFR* IC_{50}) ranging from 5-100 (for comparison, erlotinib's ratios range from 0.6-10 and osimertinib's from 2-10). In vitro, zipalertinib also demonstrates broad and deep *EGFR* inhibition by mutant/wildtype phosphorylation across structural *EGFR* mutation types that exceed other *EGFR* TKIs, including afatinib and osimertinib (Robichaux *Nature* 2021).

Clinical Data
Zipalertinib is being evaluated as monotherapy in REZILIENT 1, a phase 1/2 trial for those with NSCLC *EGFR* Ex20ins mutations treated second-line and beyond, and in combination with chemotherapy in REZILIENT 3, a global phase 3 study evaluating first-line treatment in patients with NSCLC *EGFR* Ex20ins mutations. REZILIENT 2 is a single arm phase 2 study which includes several cohorts; cohort B is evaluating first-line zipalertinib monotherapy for those with *EGFR* Ex20ins mutations (who are ineligible to receive chemotherapy); Cohort C is evaluating patients harboring *EGFR* Ex20ins or other uncommon single and compound mutations and active brain metastases or leptomeningeal disease. Patients may or may not have had prior treatment for advanced disease. Cohort D is evaluating other non-Ex20ins *EGFR* uncommon/compound mutations.

Safety data from REZILIENT 1, which evaluated doses of zipalertinib ranging from 30 mg to 150 mg BID, showed that the most common adverse events (AEs) associated with zipalertinib monotherapy were rash, paronychia, diarrhea and fatigue, all of which were grade 1 or 2. Overall, most AEs were grade 1/2 with few grade 3 or higher events. As dose discontinuations were uncommon at doses below 150 mg BID, 100 mg BID was selected for further study (100 mg BID discontinuation rate 2/39, 5.1%; and 150 mg BID 2/11, 18.2%). No grade 3 or higher paronychia, rash, or diarrhea was observed at 100 mg BID. Grade 3 or higher events at the 100 mg BID dose included anemia (1 patient) and AST increase (1 patient). Treatment-emergent pneumonitis was observed in 4/73, 5.5%, patients (1 at 65 mg, 2 at 100 mg, and 1 at 150 mg) grade 1 to 3, and cases were asymptomatic or confounded by comorbid medical illness.

In the REZILIENT 1 study, zipalertinib, as a single agent in second line and beyond, exhibited an overall response rate (ORR) of 38.4% and a median duration of response (mDOR) of 10 months. Anecdotal CNS activity is available, although only 3 patients had untreated brain metastases on trial with one showing partial response (Piotrowska *J Clin Oncol* 2023). More recent data from REZILIENT 1 Phase 2b (module C) study assesses the efficacy and safety of zipalertinib in patients (*EGFR* Ex20ins) who progressed on or after amivantamab or other prior treatment. The study demonstrated an ORR of 50% in the patients who received prior amivantamab; and an ORR of 40% with mPFS 9.7 months in the overall study population. Data on brain metastases was not reported. There were no new safety signals identified and zipalertinib was well tolerated.

REZILIENT 2 and REZILIENT 3 opened in June 2023 and continue to accrue. There is currently no clinical data on the safety of the combination of zipalertinib with antibody-drug conjugates or other targeted agents.

4.0 Aim and Eligibility

Aim	Develop innovative clinical studies (Phase I/II) to help determine the efficacy and safety of zipalertinib in the treatment of NSCLC with *EGFR* mutations including Exon 20 and other uncommon/compound mutations. It is hoped proposals submitted in response to this RFP will be useful in guiding further development of the study drug. Timely dissemination of the final study results to the larger scientific community is paramount.
Geographic Scope	United States
Eligibility Criteria: Investigators from the following organizations may apply	• NCCN Member Institutions • Collaboration between NCCN Member Institutions and collaboration between NCCN Member Institutions and other US-based institutions is strongly encouraged in order to facilitate accrual of subjects from the patient population to be studied. • All submitting investigators (Primary Investigators) must be from a NCCN Member Institution, but participating investigators do not need to be from a Member Institution. ○ Note: Co-PIs must be from the same Member Institution. • Proposal submissions from junior faculty are encouraged. • Trainees may participate as a sub-investigator under appropriate mentorship from a PI at a Member Institution.

5.0 Requirements

Clinical Area:	NSCLC with *EGFR* mutations including Exon 20 and uncommon/compound mutations
Target Audience:	NCCN Member Institutions and Participating Sites
Funding Considerations:	• There is $1.9 million available for funding of all projects. • The intent is to fund 2 multi-institutional studies. All budgets must include line-item information and a robust justification. • *Please see Section 7.0 for details on maximum per project funding amounts.* • The maximum indirect (overhead) rate is 25% and *must* be included in total grant request amount. • Direct funding will include all costs including investigators' salaries. For example, $80,000 direct costs and $20,000 indirect costs for a total grant of $100,000. Any funds in excess of the limits stipulated in this section for direct funding will require detailed justification and review.

Funding Considerations (continued):	• Salaries are capped at the current NIH salary cap. • No travel or publication, editorial, or writing assistance costs will be covered. Publication submission fees can be included in the budget. • Applicants are required to disclose additional sources of funding for this project and demonstrate that funding does not overlap. • The decision relative to funding is deferred to the members of the Scientific Review Committee (SRC) as chosen by NCCN SRC and independent of the Grantor.

Areas of research interest/emphasis:	• Phase I/II clinical trials of zipalertinib within the defined clinical area including but not limited to:
	  • Combination (clinical) studies with zipalertinib are acceptable if the toxicity profile of the agent is appropriate for combination with zipalertinib
	  • There should be sufficient data in the literature (or available unpublished institutional data) or strong preclinical rationale regarding the single agent activity of the proposed combination agent so that the contribution of zipalertinib can be determined (note- if agents that are not standard of care are proposed, partnership with other companies to provide drug supply is required).
	  • Novel treatment approaches for areas of unmet need including but not limited to brain metastasis or leptomeningeal disease with clear definition(s) of how responses will be measured
	  • Trials involving early stage, locally advanced or non-metastatic disease and/or window of opportunity trials utilizing surrogate or other novel (non-survival) endpoints
	• Preference may be given to proposals which leverage novel biomarkers or correlative endpoints to inform therapy including:
	  • Understanding mechanisms of resistance
	  • Optimal sequencing of therapy
	  • Risk and toxicity management
	  • Escalation and de-escalation of therapy and/or combination therapy
	
	Adverse event reporting is mandatory for all proposals.

Areas excluded or considered out of scope:	Specific areas considered out of scope or excluded include: • Pediatric trials • Duplicative trials of ongoing or previously funded research

	• Trials that focus only on *EGFR* Exon 19 deletions or Exon 21 L858R mutations
	• Studies with overall survival (OS) as the primary endpoint
	  • Studies can have OS as a secondary endpoint
	• Combination studies with concurrent radiation therapy or currently FDA approved immune checkpoint inhibitors
	• Non-interventional biomarker studies
	• Preclinical or translational only studies
	  • Translational studies may be a correlative component of the clinical trial
	
	No studies will utilize doses of zipalertinib outside the range for which safety data are available (i.e., nothing greater than 150 mg PO BID).
	
	Proposals with safety concerns or that are duplicative of completed, ongoing, or planned studies will not be considered. A list of ongoing trials utilizing zipalertinib can be found on clinicaltrials.gov.

Study Timeframes for Approved Studies: **Study Timeframes for Approved Studies (continued):**	• Commencement (defined as first patient receiving first dose of study drug): *no later than ten (10) months* of notice of study approval. • Complete accrual: *within two (2) years* of commencement. • Reporting/Dissemination of results in Manuscript Form: *no later than nine (9) months* after study endpoint achieved. *Please note that manuscript must be submitted to NCCN and Grantor for review prior to submission for publication consideration. • Studies will be funded as described in Section 7.0 and should be designed with subject numbers commensurate with study time frames and funding. • Studies for rarer cancers or cancer subtypes, or those that require large numbers of patients for statistical power must be multi-institutional. Network affiliate studies will be considered as long as submitting PI is from an NCCN Member Institution. *Accepted studies will be held to the following time frames:* Phase I studies are expected to complete enrollment within two years of commencement. Single-arm Phase II studies are expected to explore new approaches that can be tested in larger confirmatory studies if positive results are obtained. It is expected that these studies will complete enrollment within two years of commencement. To meet this goal, single-arm Phase II trials are encouraged to be multi-institutional. Data management and monitoring of studies should be coordinated by the applying institution. Additional

	funding for the applying institution may be requested to support the additional resources required for this activity, if the study involves multi-institutional participation. Correlative laboratory studies are expected to be completed within the same time frame as the corresponding clinical trial. Correlative laboratory studies within clinical trials already supported through other mechanisms must be completed within 2 years. Randomized Phase II multi-institutional studies are expected to complete enrollment within a two-year time frame. Multi-institutional data management and monitoring of these studies should be coordinated by the applying institution. Additional funding for the applying institution may be requested to support the additional resources required for this activity. ***All studies will require documentation of the feasibility of accruing the targeted study population as well as meeting the primary endpoint within the allotted timeframe.*** *Studies that do not meet the timeframe requirements may have funds rescinded and will be required to return any and all unused funds previously disbursed.*
Selection Criteria:	Proposals will be judged based on the following criteria: • Scientific value and innovation • Potential clinical impact • Research experience of the Research Team • Inclusion of underrepresented populations in clinical research as defined by the NIH • Soundness of study design • Statistical rigor • Feasibility including reasonable assurance of achieving intended full accrual • Appropriateness of budgetary request and full justification of all direct and indirect expenses *The Grantor may reject any study with potential safety issues or if it is an already studied concept.*
Drug Supply:	Zipalertinib will be supplied by Grantor for all approved and funded studies. If the proposal requires a second investigational drug, a letter of commitment for provision of that drug by supplier must be submitted with proposal.
Key Dates:	• Original RFP release date**:** October 30, 2024; **RFP Re-release Date: January 21, 2025**

	• Original proposal submission deadline: January 6, 2025; **Extended Submission Deadline: March 18, 2025** (Please note that the submission deadline is 5:00 PM Eastern Time) • Original anticipated grant award notification date: Middle of February 2025; **Updated Anticipated Grant Award Notification Date: Middle of April 2025** • **Protocol Draft:** Due within 30 calendar days after award notification • **Commencement of Study:** Within 10 months after award notification • **Study Completion:** 2 years after commencement • **Manuscript Draft:** Within 9 months after completion
Questions:	If you have questions regarding this RFP, please direct them in writing to Nicole Zion, Senior Manager, Clinical Research, at Zion@nccn.org with the subject **"NCCN Taiho NSCLC RFP"**.

6.0 Review and Approval Process

The NCCN Request for Proposals Development Team (RFPDT) has developed a Request for Proposals (RFP) with a formalized review procedure to accept applications and select the proposals of highest scientific merit. The NCCN RFPDT has overseen the development of the RFP and the NCCN Scientific Review Committee composed of this group will perform the review of applications. All reviews, evaluations and award decisions are independent of Grantor.

Applicants will be notified via email with the notification of funding status by the dates noted above.

Proposals duplicative of completed, ongoing, or planned studies will not be considered. If you need additional information or have questions, please e-mail Nicole Zion, Senior Manager, Clinical Research, at Zion@nccn.org or call 215-690-0230.

Studies that have safety issues, are already well-funded concepts, or are not consistent with the strategy for investigation as written in this RFP will not be reviewed by the SRC.

7.0 Funding

NCCN and its Member Institutions have an agreement to include a maximum of 25% indirect costs for trials funded by the NCCN. Direct funding will include all costs including investigators' salaries. For example, $80,000 direct costs and $20,000 indirect costs for a total grant of $100,000.

Total funding is not to exceed $950,000. All budgets must include line-item information and a robust justification.

Funding will be disbursed to approved studies as follows:

Phase I trials:

- 15% of total award for such study after IRB approval and dosing of first study subject;
- Based on the per study subject costs, after the initial 15% of funding has been accounted for based on study subject accrual, funds will be awarded on a quarterly basis for eligible study subjects enrolled in a study, based on the per study subject rate up to a maximum of an additional 65% of the funding; and
- 20% of funds will be awarded after submission of a manuscript for publication.

Phase II trials:

- 15% after IRB approval and dosing of first study subject;
- Based on the per study subject costs, after the initial 15% of funding has been accounted for based on Study Subject accrual, funds will be awarded on a quarterly basis for eligible study subjects enrolled in a study, based on the per study subject rate up to a maximum of an additional 65% of the funding; and
- 20% after submission of a manuscript for publication.

Phase II trials with 2-Stage Design with Early Stopping Rules:

- 15% of total requested funding (based on maximum number of anticipated study subjects) after IRB approval and dosing of first study subject;
- Remainder of per Study Subject funding for the number of study subjects in the first stage after all study subjects are accrued to the first stage of a study (total funding for the number of study subjects in first stage less the initial payment) up to a maximum of an additional 65% of the funding;
- Total per study subject funding for the number of study subjects in the second stage less final payment after all study subjects are accrued to the second stage; and
- 20% of total requested funding (based on maximum number of anticipated study subjects) after submission of a manuscript for publication.

Multi-center Randomized Phase II Study(ies):

- 15% after IRB approval and dosing of first study subject;
- Based on the per study subject costs, after the initial 15% of funding has been accounted for based on study subject accrual, funds will be awarded on a quarterly basis for eligible study subjects enrolled in a study, based on the per study subject rate up to a maximum of an additional 65% of the funding;
- 20% after submission of a manuscript for publication; and
- Any additional funding will be disbursed to the coordinating center for data management and monitoring. These funds will be delegated at the discretion of the lead Principal Investigator and may include outsourcing of data management and/or monitoring to an independent research organization.

Studies that do not meet the time frame requirements as stipulated in Section 5.0 will have funds rescinded and will be required to return any and all unused funds previously disbursed.

8.0 Proposals

In order to respond to the RFP, investigators will submit a proposal in the format delineated below to NCCN, which will be evaluated by the NCCN Scientific Review Committee (SRC).

Proposals are required to be submitted electronically to the NCCN research portal at https://nccn.envisionpharma.com/ienv_nccn and include a letter of support from the governing groups of the institution verifying:

1) Office of Sponsored Research approval
2) Department Chair/Division approval
3) Institutional budgetary review and approval
4) The priority status of the research stating if there are competing trials. If there are competing trials, please verify that this trial will have a higher priority.
5) Documentation to support feasibility of clinical trials with at least one of the following:
    - Letter from institution's Feasibility Committee, if applicable
    - Documentation by previous studies and accrual (if available, publications and abstracts)
6) Letter(s) of support from participating institutions including name of PI at participating institution and their feasibility

Letters should be addressed to Crystal S. Denlinger, MD, FACP, CEO, National Comprehensive Cancer Network, 3025 Chemical Road, Suite 100, Plymouth Meeting, PA 19462.

Proposals will provide concise documentation of the research plan and should be the equivalent of no more than 10 pages. The proposal is expected to contain sufficient information to allow the reviewers to fully assess the scientific rigor of the proposed study. A full research project plan may be submitted as an attachment but the required information in iEnvision must also be completed. A robust review of the statistical plan will be conducted.

Proposals should contain detailed information regarding the following areas:

8.1 Clinical Trials

A. General Information: Title/Type of Support/Subsite(s)
    - Select "**ZIPA**" for RFPID
    - Select "**Funding and Product**" for Type of Support

B. Investigators and institutional affiliations
    - Include academic title and rank

C. Site Information
    - Primary and sub-site information as applicable

D. Concept information
    - Enrollment/Design/Phase
    - Estimated time of completion
    - Overview/Hypothesis

- Background/Rationale

E. Scientific summary
   - Primary/Secondary objectives
   - Primary/Secondary endpoints
   - Inclusion/Exclusion criteria
   - Study population
   - Sample size/Statistical analysis
   - Treatment plan
   - References

F. Oncology analysis
   - Tumor Type/Stage/Body systems
   - Correlative study information
   - Select “no” from dropdown box
   - Outcome measures
   - Feasibility documentation
   - Letter of Support

G. Request for product: Formulation Dosage/Quantity

H. Planned publications: Journal/Congress/Anticipated Dates

8.2 **Requested Funding Information** (See iEnvision User Manual for additional instructions)

A. Complete the **NCCN Budget Template** (attached) and submit the **full budget** via the attachments folder.
   - Breakdown costs by major cost categories
   - Provide justification of major costs with enough detail to demonstrate how funding for major elements in the study will be allocated
   - Salaries are capped at the current NIH salary cap
   - No travel or publication costs will be covered

B. Complete the remainder of the Funding Page:
   - Total direct and indirect costs (see instructions)
   - Requested currency (US Dollar)
   - Overhead %
   - Amount Requested
   - Additional sources of funding

8.3 Required Documentation for Combination Treatment
<u>This documentation must be provided to NCCN along with the proposal or it will not be considered for funding.</u>

A. Documentation of the availability of the other agent is required if zipalertinib is to be studied in combination with an agent from another pharmaceutical company, used outside its indication, or obtained as standard of care.

B. If zipalertinib will be studied in combination with an investigational/approved agent, obtained from a pharmaceutical company, the investigator must provide letter stating the following:
    i. The company's commitment to provide drug for the investigation;
    ii. The agreement of that company to allow presentation and publication of results, and
    iii. The agreement of that company to allow cross-filing or filing of a new IND.
C. If zipalertinib will be studied in combination with an agent used outside of its indication, the investigator must provide documentation of how they are obtaining the drug.

8.4 Ancillary Documentation
A. Curriculum Vitae (CV) for the Principal Investigator
B. An appendix of supportive literature may be provided
C. Any additional information to support proposal submission

9.0 Proposal Submission Process

9.1 Submission

All proposals must be submitted electronically using the directions below and are due by **5:00 PM (EST) on March 18, 2025.** No exceptions will be granted.

A. Please use the link below to register in the system:
    i. https://nccn.envisionpharma.com/ienv_nccn
B. Select "Register for New Account" in the upper right corner of the page, above the "Log In" button
C. Complete all fields (Note: Fields with an asterisk are required)
D. You will receive a confirmation email. Click on the link in the email to activate your account.
E. Enter your username and password (Note: Your username is your email address. Do not copy and paste.)
F. Set up your security questions
G. Submit your study

For technical assistance with the iEnvision system, please contact helpdesk@envisionpharmasupport.com.

For questions or issues, please email Nicole Zion at zion@nccn.org with the subject line "NCCN Taiho NSCLC RFP". NCCN will seek to provide information to potential investigators regarding ongoing or completed studies of zipalertinib in order to avoid the submission of a proposal that is already a well-studied concept.

10.0 Additional Terms and Conditions

10.1 Human Biological Specimens: All specimens must be obtained under informed consent and IRB approval appropriate for the study. Compliance with all federal regulations is required.

10.2 Protocol and IRB submission:

10.2(a) Draft protocols will be reviewed by NCCN and the Grantor **prior** to IRB review. **A copy of the draft protocol must be submitted to NCCN within 4 weeks after the study approval letter.** The protocol must be consistent with the approved proposal and all reviewer comments must be addressed.

10.2(b) All investigators will submit protocols for IRB review and document approval to NCCN prior to study activation and all collaborators will furnish evidence of IRB approval. It is expected that IRB review and approval be completed **within 150 days** following NCCN notification of funding for the project.

10.3 IACUC review and approval: All investigators conducting animal experiments will submit research project plans for IACUC review and document approval to NCCN prior to study activation. It is expected that IACUC review and approval be completed **within 90 days** following NCCN notification of funding for the project.

10.4 Serious Adverse Event Reporting: All serious adverse events will be reported to NCCN and the Grantor in addition to local regulatory authorities.

10.5 Institutional Monitoring: All studies will be internally monitored in accordance with appropriate committees (e.g. institutional Data Safety and Monitoring Plan in the case of human studies). A copy of the Data Monitoring Plan for the study must be submitted to NCCN prior to NCCN approval of study activation.

10.6 IND:

10. 6(a) Investigators are required to hold INDs for studies but will be allowed to cross-reference a filing to Grantor's IND. Investigators are encouraged to apply to the FDA for IND exemption if studies meet all criteria according to 21 CFR 312.2(b). A copy of the FDA approval letter for IND exemption must be submitted to NCCN before study drug will be released.

10.6(b) Proposals using an experimental diagnostic imaging agent that will require an IND must outline how regulatory issues will be handled in order to meet the required study time frame.

10.7 Progress Reports: Investigators will provide interim progress reports to NCCN detailing the progress of studies quarterly, and upon study completion. These reports will be used administratively for funding purposes. If study progress or accrual lags behind the expected rate, the SRC may be asked for suggestions to improve study progress, or alternatively, to terminate the study and any further funding.

10.8 Specimen Transmittal: If specimens are to be transported extramurally for collaborative laboratory studies, all institutional requirements for safety and confidentiality will be met.

10.9 Abstracts and Publications: Abstracts for presentation at scientific meetings and all publications of study results will be submitted to NCCN and Grantor for review related to protection of company's intellectual property and confidential information **prior to any submission**. Abstracts must be submitted at least 10 days prior to submission and manuscripts at least 30 days prior to submission. Grantor may delay publication and disclosure of the manuscript or abstract for up to an additional sixty (60) days so as to seek patent protection of intellectual property rights.

10.10 NCCN Multi-Institutional Studies: Collaborative studies between NCCN Member Institutions are encouraged. For these studies, the proposal feasibility section should provide information about data management, statistical analysis, and specimen handling issues. Additional funding may be provided for centralized data management and monitoring by the applying institution.

10.11 NCCN institutions and investigators will be responsible for conducting all studies in accordance with the applicable research plan, GCP Guidelines, and all applicable laws and regulations. NCCN institutions and investigators will be responsible for all data collection, statistical analysis and safety reporting.

10.12 Investigators must provide reasonable assurance that submitted studies will be able to reach completion within the time frames specified in Section 5.0.

10.13 Final protocols must be consistent with approved proposals. Funds will be rescinded if there are significant changes without prior NCCN approval. There will be no exceptions.

10.14 The Principal Investigator (PI) listed on the protocol must be the same PI listed on the proposal submission unless approved by NCCN.

11.0 Study Agreement

A study agreement will be signed between NCCN and each participating institution.

If an institution requires a separate agreement with another pharmaceutical company for a study, that agreement must be fully executed by the time of final agreement execution with NCCN.

All aforementioned points between NCCN and the participating institution must be strictly adhered to.

12.0 References

1. Robichaux JP, Le X, Vijayan RSK, Hicks JK, Heeke S, Elamin YY, Lin HY, Udagawa H, Skoulidis F, Tran H, Varghese S, He J, Zhang F, Nilsson MB, Hu L, Poteete A, Rinsurongkawong W, Zhang X, Ren C, Liu X, Hong L, Zhang J, Diao L, Madison R, Schrock AB, Saam J, Raymond V, Fang B, Wang J, Ha MJ, Cross JB, Gray JE, Heymach JV. Structure-based classification predicts drug response in EGFR-mutant NSCLC. Nature. 2021 Sep;597(7878):732-737. doi: 10.1038/s41586-021-03898-1. Epub 2021 Sep 15. PMID: 34526717; PMCID: PMC8481125

2. Zofia Piotrowska et al., Safety, Tolerability, and Antitumor Activity of Zipalertinib Among Patients With Non–Small-Cell Lung Cancer Harboring Epidermal Growth Factor Receptor Exon 20 Insertions. JCO 41, 4218-4225(2023). DOI:10.1200/JCO.23.00152
3. A. Passaro, H.A. Yu, D. Nguyen, V.H.F. Lee, R.A. Soo, S.H. Kim, H. Daga, D.S.W. Tan, S. Kim, O.J. Juan Vidal, Z. Piotrowska, E.K. Keeton, T. Liu, S. Li, J. Jones, G. Ruiter, Safety and anti-tumour activity of zipalertinib in NSCLC patients (pts) with EGFR exon 20 insertion (ex20ins) mutations who received prior amivantamab. Annals of Oncology (2024) 35 (suppl_2): S802-S877. 10.1016/annonc/annonc1602