Pemigatinib (FGFR)

Near-term opportunities in multiple tumor types

September 27, 2019

Speakers on Today’s Webcast

- **Hervé Hoppenot**
  Chief Executive Officer
  Incyte

- **Steven Stein, MD**
  Chief Medical Officer
  Incyte

Forward-looking Statements

Except for the historical information set forth herein, the matters set forth in this presentation contain predictions, estimates and other forward-looking statements, including without limitation statements regarding: expectations regarding the timing of clinical trial results, and whether those results will demonstrate sufficient efficacy to continue development or seek or obtain regulatory approval, for ruxolitinib in GVHD, pemigatinib in cholangiocarcinoma, bladder cancer and solid tumors, itacitinib in GVHD, parsaclisib in lymphomas, INCMGA0012 in various cancers and ruxolitinib cream for vitiligo and atopic dermatitis; expectations regarding the timing of the filing of an NDA for pemigatinib in cholangiocarcinoma; expectations for our pemigatinib development program, including planned initiations of studies, expected time for enrollment, expected timing of results, whether any of these studies will achieve any or all of their endpoints, and whether and when any regulatory submissions for any of the potential indications will occur; and the potential commercial opportunities for pemigatinib.

These forward-looking statements are based on our current expectations and are subject to risks and uncertainties that may cause actual results to differ materially, including unanticipated developments in and risks related to: unanticipated delays; further research and development and the results of clinical trials possibly being unsuccessful or insufficient to meet applicable regulatory standards or warrant continued development; the ability to enroll sufficient numbers of subjects in clinical trials; determinations made by the FDA or other regulatory authorities around the world; the efficacy or safety of our products and the products of our collaboration partners; the acceptance of our products and the products of our collaboration partners in the marketplace; market competition; sales, marketing, manufacturing and distribution requirements; unanticipated variations in demand for products; greater than expected expenses; expenses relating to litigation or strategic activities; government activities, including potential new laws and regulations, affecting the healthcare market generally and the pharmaceutical and biotech industries specifically; and other risks detailed from time to time in our reports filed with the U.S. Securities and Exchange Commission, including our quarterly report on Form 10-Q for the quarter ended June 30, 2019. We disclaim any intent or obligation to update these forward-looking statements.

Incyte has Six Late-Stage Development Programs

Hematology & Oncology

ruxolitinib[1] (JAK1/JAK2)	itacitinib (JAK1)	pemigatinib (FGFR1/2/3)	parsaclisib (PI3Kδ)	INCMGA0012 (PD-1)
steroid-refractory acute GVHD, steroid-refractory chronic GVHD	steroid-naïve acute GVHD, steroid-naïve chronic GVHD	cholangiocarcinoma, bladder cancer, 8p11 MPN, solid tumors	follicular lymphoma, mantle cell lymphoma, marginal zone lymphoma	MSI-high endometrial cancer, anal cancer, Merkel cell carcinoma
3,000 new patients per year in US	**15,000 new patients per year**	**35,000 new patients per year**	**22,000 new patients per year (2L+)**	**15,000 new patients per year**
2019: Phase 3 results in both indications expected	**2019:** Phase 3 results in acute GVHD expected	**2019:** cholangiocarcinoma NDA filing expected	**2020:** Initial data expected	**2020:** Initial data expected

IAI

ruxolitinib cream (JAK1/JAK2)
atopic dermatitis, vitiligo
~12 million potential patients in the US
2019: Phase 3 initiated in vitiligo

1. Development of ruxolitinib in GVHD in collaboration with Novartis.
All epidemiology data for US, Europe and Japan except where noted for US only; all incidence data for unresectable or metastatic disease, except prevalence data for ruxolitinib cream.
References upon request.

Pemigatinib Represents an Important Near-Term Opportunity

Hematology & Oncology

ruxolitinib[1] (JAK1/JAK2)	itacitinib (JAK1)	pemigatinib (FGFR1/2/3)	parsaclisib (PI3Kδ)	INCMGA0012 (PD-1)
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References upon request.

Pemigatinib is a Selective, Potent, Oral Inhibitor of FGFR1, 2, and 3

	Pemigatinib[1] (INCB54828)	Erdafitinib[2] (JNJ-42756493)	Rogaratinib[3,4] (BAY1163877)	Infigratinib[5,6] (BGJ398)	Derazantinib[7,8] (ARQ087)	Futibatinib[9,10] (TAS-120)
FGFR1 IC_{50} (nM)	**0.4**	1.2	15	0.9	4.5	3.9
FGFR2 IC_{50} (nM)	**0.5**	2.5	<1	1.4	1.8	1.3
FGFR3 IC_{50} (nM)	**1**	3	19	1.0	4.5	1.6
FGFR4 IC_{50} (nM)	**30**	5.7	33	60	34	8.3
VEGFR2 IC_{50} (nM)	**71**	36.8	120	180	21	UNK
Dosing	13.5 mg QD	8 mg QD	800 mg BID	125 mg QD	300 mg QD	20 mg QD

Desired target activity

Off-target activity

1. Liu PCC, et al. AACR 2015. Poster 771; 2. Perera TPS, et al. Mol Cancer Ther. 2017;16:1010-1020; 3. Joerger M, et al. ASCO 2018. Abstract 4513; 4. Collin MP, et al. ChemMedChem. 2018 Mar 6;13(5):437-445; 5. Guagnano V, et al. *J Med Chem*. 2011;54:7066-7083; 6. Nogova L, et al. *J Clin Oncol*. 2017;35:157-165; 7. Hall T, et al. *PLoS ONE*. 2016;11:e0162594; 8. Papadopoulos KP, et al. *Br J Cancer*. 2017;117(11):1592-1599; 9. Babina IS, Turner NC. *Nat Rev Cancer*. 2017;17(5):318-332; 10. Meric-Bernstam F, et al. ESMO GI 2018, abstract O-001

Executing a Broad Development Plan across Multiple Tumor Types

Cholangiocarcinoma

- ✓ Pivotal trial initiated, 1L vs gem/cis
- Planned NDA submission, 2L
  Breakthrough therapy designation

Bladder cancer

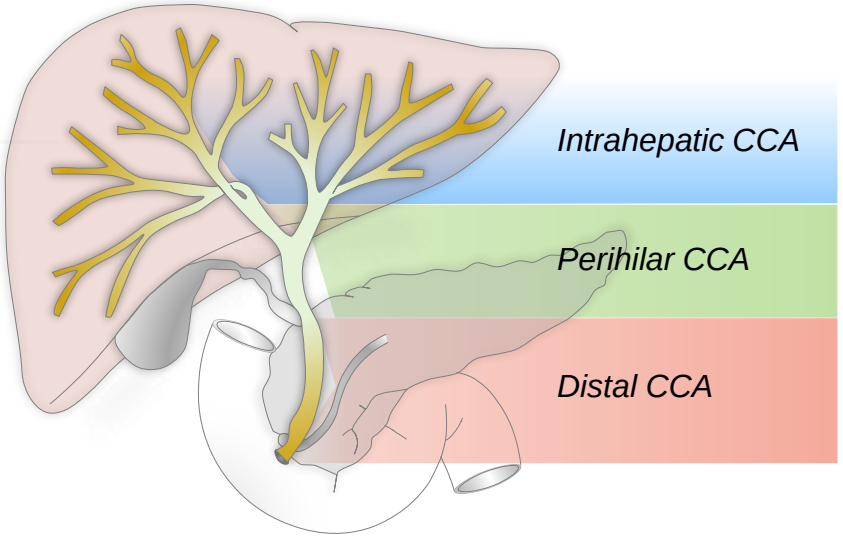
- Complete recruitment, 2L
  Continuous dosing cohort
- Initiate trial, 1L
  vs standard of care
- Planned sNDA submission, 2L

Solid tumor agnostic

- Initiate development program, 2L
  Continuous dosing

Cholangiocarcinoma: Heterogeneous Tumors Arising in the Bile Duct

- Cholangiocarcinomas (CCAs) are epithelial tumors arising from the biliary tree[1-3]
- Most common primary malignancy of the bile duct
- Heterogeneous tumors that are classified into 3 anatomical subtypes:
  - Intrahepatic
  - Perihilar
  - Distal

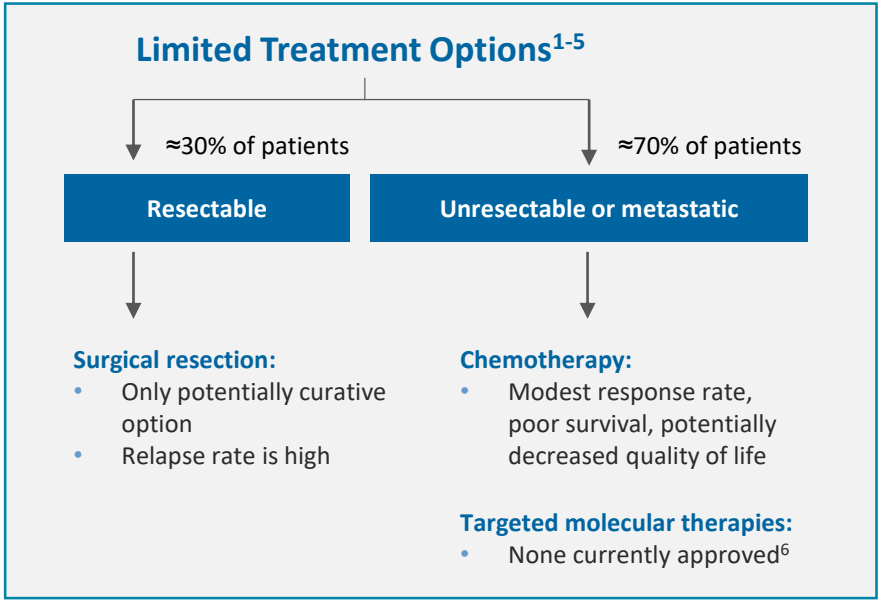


- No well established treatment following failure of gemcitabine/cisplatin
- Second line chemotherapies[4-7]:
  - ORR: <10%
  - median PFS: ~3 months
  - median OS: 6–7 months

1. Rizvi S, Gores GJ. *J Hepatol.* 2017;67(3):632-644; 2. Ghouri YA. *J Carcinog.* 2015;14:1; 3. Farshidfar F, et al. *Cell Rep*. 2017;18(11):2780-2794; 4. Goff LW, et al. J Clin Oncol. 2016;34:e15636. 5. Lamarca A, et al. J Clin Oncol. 2019;37(15 Suppl):4003 [abstract]. 6. Ying J, Chen J. Crit Rev Oncol Hematol. 2019;139:134–42.
7. Lowery MA, et al. Cancer. 2019 Aug 27. doi: 10.1002/cncr.32463

Prognosis of Patients Diagnosed With Cholangiocarcinoma is Poor

- Surgical resection is the only potentially curative therapy for CCA,[1] however:
  - Approximately **70%** of patients are diagnosed with unresectable disease[1]
  - Relapse rate is high in patients who undergo surgery[1]
- The 5-year survival rate of CCA patients ranges between **5% to 15%**[1]
- For patients with unresectable or metastatic CCA, median survival is **<1 year**[2]



1. Valle JW et al. *Cancer Discov.* 2017;7(9):943-962. 2. Valle J, et al. *N Engl J Med.* 2010;362(14):1273–1281. 3. Banales JM, et al. *Nat Rev Gastroenterol Hepatol*. 2016;13:261–280. 4. Macias RIR. *ISRN Hepatol*. 2014; 2014:828074. 5. Moehler M, et al. *Eur J Cancer*. 2014;50:3125–3135. 6. Rizvi S, Borad MJ. *J Gastrointest Oncol*. 2016;7:789–796.

BARCELONA 2019 ESMO congress

FIGHT-202: A PHASE 2 STUDY OF PEMIGATINIB IN PATIENTS WITH PREVIOUSLY TREATED LOCALLY ADVANCED OR METASTATIC CHOLANGIOCARCINOMA

Vogel A,[1] Sahai V,[2] Hollebecque A,[3] Vaccaro G,[4] Melisi D,[5] Al-Rajabi R,[6] Paulson AS,[7] Borad MJ,[8] Gallinson D,[9] Murphy AG,[10] Oh D-Y,[11] Dotan E,[12] Catenacci DV,[13] Van Cutsem E,[14] Lihou C,[15] Zhen H,[15] Féliz L,[15] Abou-Alfa GK[16,17]

[1]Hannover Medical School, Hannover, Niedersachsen, Germany; [2]University of Michigan, Ann Arbor, MI, USA; [3]Gustave Roussy, Villejuif, France; [4]Providence Cancer Center Oncology and Hematology Care Clinic, Portland, OR, USA; [5]Università degli studi di Verona, Verona, Italy; [6]University of Kansas Cancer Center, Kansas City, KS, USA; [7]Baylor Charles A. Sammons Cancer Center, Baylor University Medical Center, Dallas, TX, USA; [8]Mayo Clinic Cancer Center, Scottsdale, AZ, USA; [9]Morristown Memorial Hospital, Carol Cancer Center, Morristown, NJ, USA; [10]Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University School of Medicine, Baltimore, MD, USA; [11]Seoul National University Hospital, Seoul National University College of Medicine, Seoul, South Korea; [12]Fox Chase Cancer Center, Philadelphia, PA, USA; [13]University of Chicago Medicine, Chicago, IL, USA; [14]University Hospitals Leuven and KU Leuven, Leuven, Belgium; [15]Incyte Corporation, Wilmington, DE, USA; [16]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [17]Weill Medical College at Cornell University, New York, NY, USA

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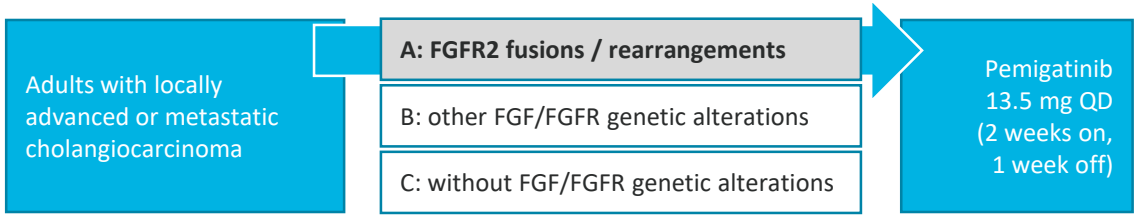
FIGHT-202: Study Design and Clinical Characteristics



Characteristics	Cohort A (n = 107) *FGFR2* Fusions/ Rearrangements	Cohort B (n = 20) Other *FGF/FGFR* Genetic Alterations	Cohort C (n = 18) No *FGF/FGFR* Genetic Alterations	Total (N = 146)*
ECOG PS, n (%)				
0	45 (42)	7 (35)	7 (39)	59 (40)
1	57 (53)	10 (50)	8 (44)	76 (52)
2	5 (5)	3 (15)	3 (17)	11 (8)
Number of prior regimens,† n (%)				
1	65 (61)	12 (60)	12 (67)	89 (61)
2	29 (27)	7 (35)	2 (11)	38 (26)
≥3	13 (12)	1 (5)	4 (22)	19 (13)
Prior cancer surgery, n (%)	38 (36)	6 (30)	4 (22)	48 (33)
Prior radiation, n (%)	28 (26)	3 (15)	5 (28)	36 (25)
CCA location, n (%)				
Intrahepatic	105 (98)	13 (65)	11 (61)	130 (89)
Extrahepatic	1 (1)	4 (20)	7 (39)	12 (8)
Other/Missing	1 (1)	3 (15)‡	0	4 (3)

Primary endpoint:
Independently-confirmed ORR in cohort A (patients with FGFR2 fusions or rearrangements)

Secondary endpoints:
ORR in cohorts B, A+B, and C
Duration of response; disease control rate; progression-free survival; overall survival and safety in all cohorts

fight-202

* The total includes 1 patient who received pemigatinib but had undetermined FGF/FGFR status; analyzed for safety but not efficacy, and was not assigned to a cohort.
† Maximum number of 5 therapies in cohort A and 3 in cohort B/C.
‡ Other includes gallbladder (n = 2) and ampulla of vater (n = 1) cancer.

FIGHT-202: Adverse Events Occurring in ≥25% of Patients

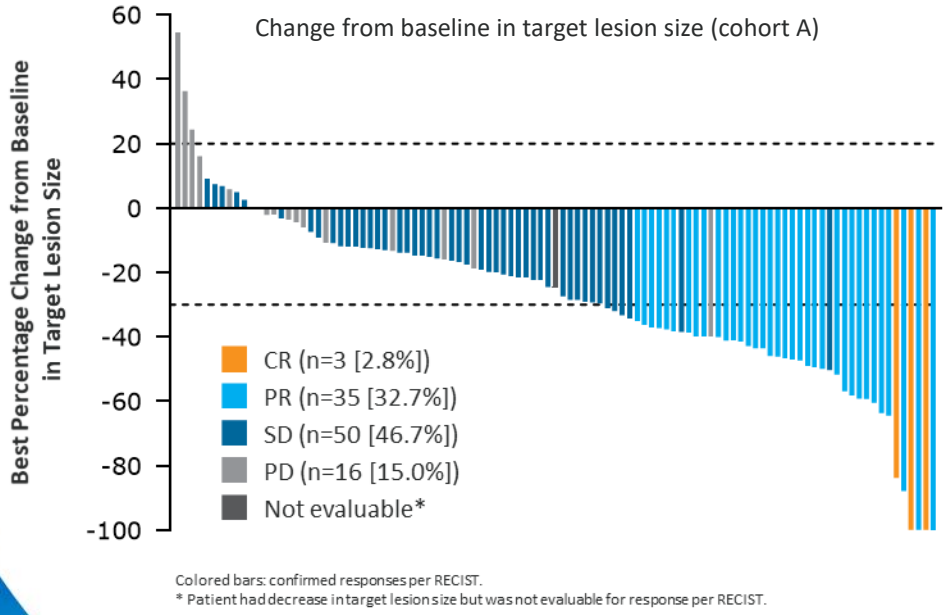
Adverse Event, n (%)	Any AEs (N = 146)*	
	All Grades	Grade ≥3
Hyperphosphatemia†	88 (60)	0
Alopecia	72 (49)	0
Diarrhea	68 (47)	4 (3)
Fatigue	62 (42)	7 (5)
Nail toxicities†	62 (42)	3 (2)
Dysgeusia	59 (40)	0
Nausea	58 (40)	3 (2)
Constipation	51 (35)	1 (1)
Stomatitis	51 (35)	8 (5)
Dry mouth	49 (34)	0
Decreased appetite	48 (33)	2 (1)
Vomiting	40 (27)	2 (1)
Dry eye	37 (25)	1 (1)
Arthralgia	36 (25)	9 (6)

- Hyperphosphatemia† managed with a low phosphate diet, phosphate binders, and diuretics, or dose reduction/interruption
  - All grade 1 or 2
  - Few (n=3) required dose reductions/interruptions
- Hypophosphatemia† occurred in 23% of patients
  - Most common grade ≥3 AE (12%)
  - None clinically significant/serious; none led to discontinuation/dose reduction
- Serous retinal detachment† occurred in 4% of patients
  - Mostly grade 1/2 (grade ≥3, 1%)
  - None resulted in clinical sequelae

* Safety analysis includes 1 patient who did not have confirmed FGF/FGFR status by central laboratory and was not assigned to any cohort.
† Combined MedDRA Preferred Terms.

FIGHT-202: Efficacy by Independent Central Review

ORR of 36% with durable responses in previously treated patients



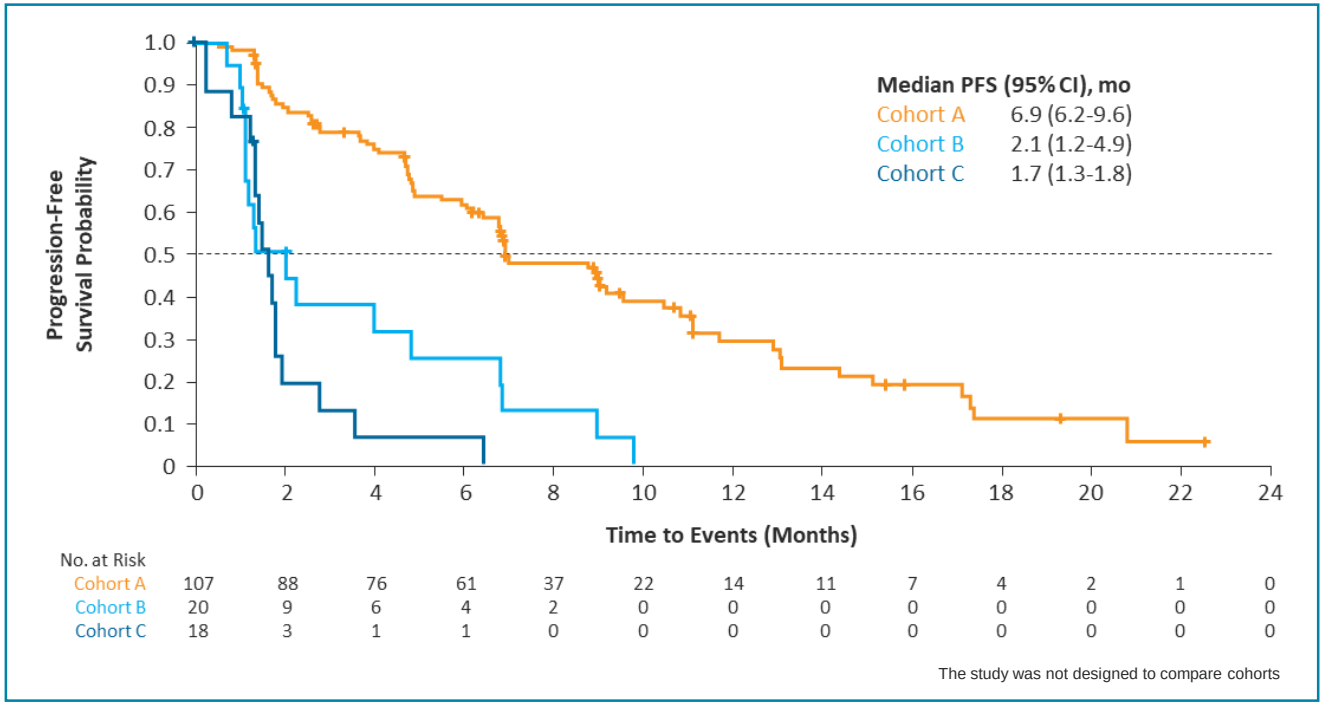
Colored bars: confirmed responses per RECIST.
* Patient had decrease in target lesion size but was not evaluable for response per RECIST.

Variable	Cohort A (n = 107)	Cohort B (n = 20)	Cohort C (n = 18)
ORR (95% CI), %	**35.5** (26.50–45.35)	0	0
Best OR,* n (%)			
CR	3 (2.8)	0	0
PR	35 (32.7)	0	0
SD	50 (46.7)	8 (40.0)	4 (22.2)
PD	16 (15.0)	7 (35.0)	11 (61.1)
Not evaluable†	3 (2.8)	5 (25.0)	3 (16.7)
Median DOR (95% CI), mo	**7.5** (5.7–14.5)	—	—
DCR (CR + PR + SD) (95% CI), %	**82** (74–89)	40 (19–64)	22 (6–48)

* Assessed and confirmed by independent central review.
† Postbaseline tumor assessment was not performed owing to study discontinuation (2 participants in cohort A, 4 participants in cohort B, 3 participants in cohort C) or was performed prior to the minimum interval of 39 days for an assessment of SD (1 participant in cohort A, 1 participant in cohort B).

FIGHT-202: Efficacy by Independent Central Review

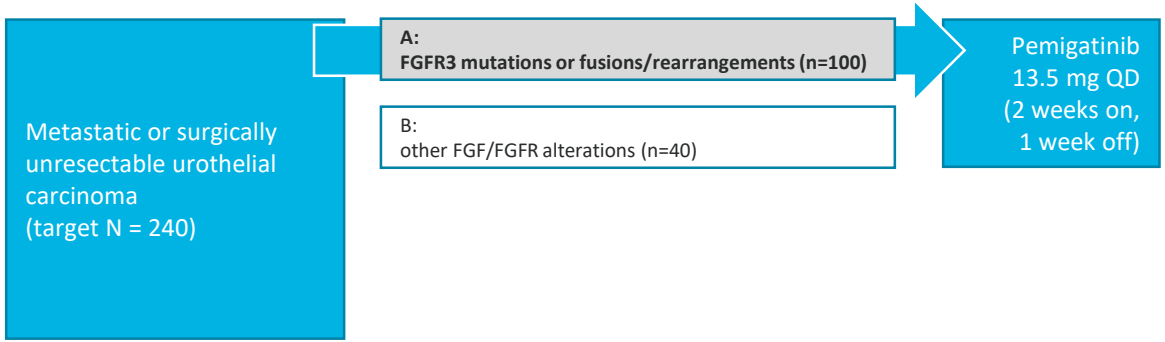
Median PFS ~7 months in previously treated patients



	Cohort A	Cohort B	Cohort C
Median (range) duration of follow-up, mo	15.4 (7.0–24.7)	19.9 (16.2–23.5)	24.2 (22.0–26.1)
Median (range) duration of treatment, mo	7.2 (0.2–24.0)	1.4 (0.2–12.9)	1.3 (0.2–4.7)

Pemigatinib also Under Evaluation in Patients with Bladder Cancer

FIGHT-201



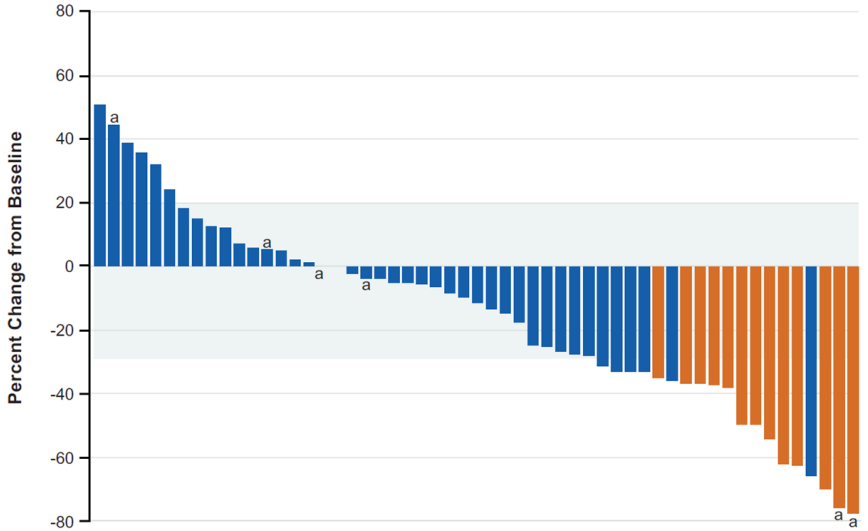
Primary endpoint:
ORR in patients with FGFR3 mutations and fusions/rearrangements

Secondary endpoints:
ORR in patients with other FGF/FGFR alterations
Progression-free survival and duration of response
Safety and tolerability

FIGHT-201: Safety & Efficacy to Date

More intensive treatment regimen may increase efficacy, hence move to continuous dosing

Best percent change from baseline in target lesion size in patients with UC and FGFR3 mutations/fusions (Cohort A)[1]



Orange bars = partial response. [a] FGFR3 fusions.

Most common TEAEs[a] that occurred in ≥ 20% of patients[1]

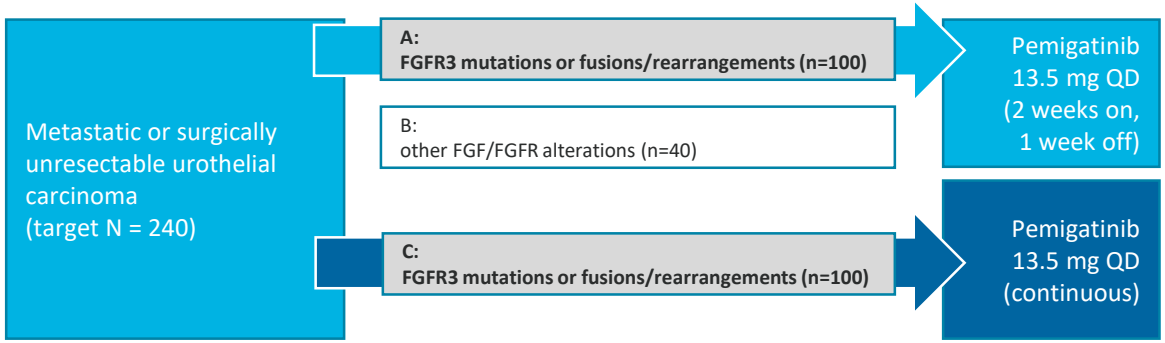
	Total (N = 108)	
Events, n (%)	All Grades	Grade ≥ 3
Diarrhea	47 (43.5)	3 (2.8)
Alopecia	43 (39.8)	1 (0.9)
Constipation	38 (35.2)	1 (0.9)
Stomatitis	37 (34.3)	8 (7.4)
Fatigue	35 (32.4)	6 (5.6)
Dry Mouth	35 (32.4)	1 (0.9)
Hyperphosphatemia[b]	34 (31.5)	1 (0.9)
Decreased appetite	32 (29.6)	4 (3.7)
Dysgeusia	32 (29.6)	0 (0)
Nausea	28 (25.9)	1 (0.9)
Asthenia	27 (25.0)	4 (3.7)
Abdominal Pain	25 (23.1)	3 (2.8)
Back Pain	22 (20.4)	4 (3.7)

a Patients were counted once under MedDRA preferred term.
b Hyperphosphatemia was managed with phosphate binder, diet, and/or dose interruption.

1. Necchi A, et al. ESMO 2018. Poster 900P.

Continuous Dosing Cohort to Complete Recruitment by End 2019

fight-201



Primary endpoint:
ORR in patients with FGFR3 mutations and fusions/rearrangements

Secondary endpoints:
ORR in patients with other FGF/FGFR alterations
Progression-free survival and duration of response
Safety and tolerability

First-Line Bladder Trial is Being Initiated, versus Standard of Care

fight-205

Metastatic or unresectable urothelial carcinoma in cisplatin-ineligible participants whose tumors express FGFR3 mutation or fusions/rearrangements

(target N = 372)

- **Pemigatinib + pembrolizumab**
- **Pemigatinib**
- Standard of care (chemotherapy[1] or pembrolizumab)

Primary endpoint:
Progression-free survival

Secondary endpoints:
Overall survival, objective response rate, duration of response, safety, quality of life

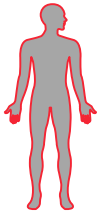
1. gemcitabine in combination with carboplatin

Tumor-Agnostic Development is an Important Next Step for Pemigatinib

Site-based treatments

Lung cancer
Chemotherapy

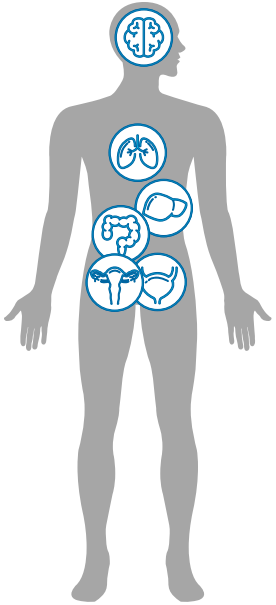
Melanoma
Chemotherapy



Biomarker-driven approaches

Lung cancer
ALK translocations

Melanoma
BRAF mutations



Tumor-agnostic biomarker approaches

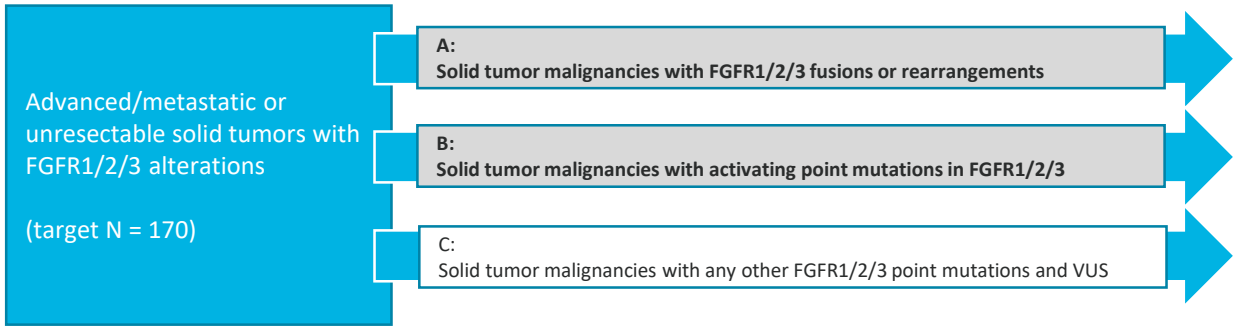
Pemigatinib
FGFR alterations

Pembrolizumab
dMMR / MSI-H; FDA approved 2017

Larotrectinib
NTRK; FDA approved 2018

The Tumor-Agnostic Trial for Pemigatinib is Now Open

FIGHT-207



Primary endpoint:
Objective response rate (cohorts A and B)

Secondary endpoints:
Progression-free survival, duration of response, overall survival, safety

VUS = variants of unknown significance.

Initial Submission for Approval of Pemigatinib is Expected in H2 2019

Potential to be first FGFR inhibitor FDA-approved for cholangiocarcinoma

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Multiple subsequent opportunities in patients with FGFR alterations

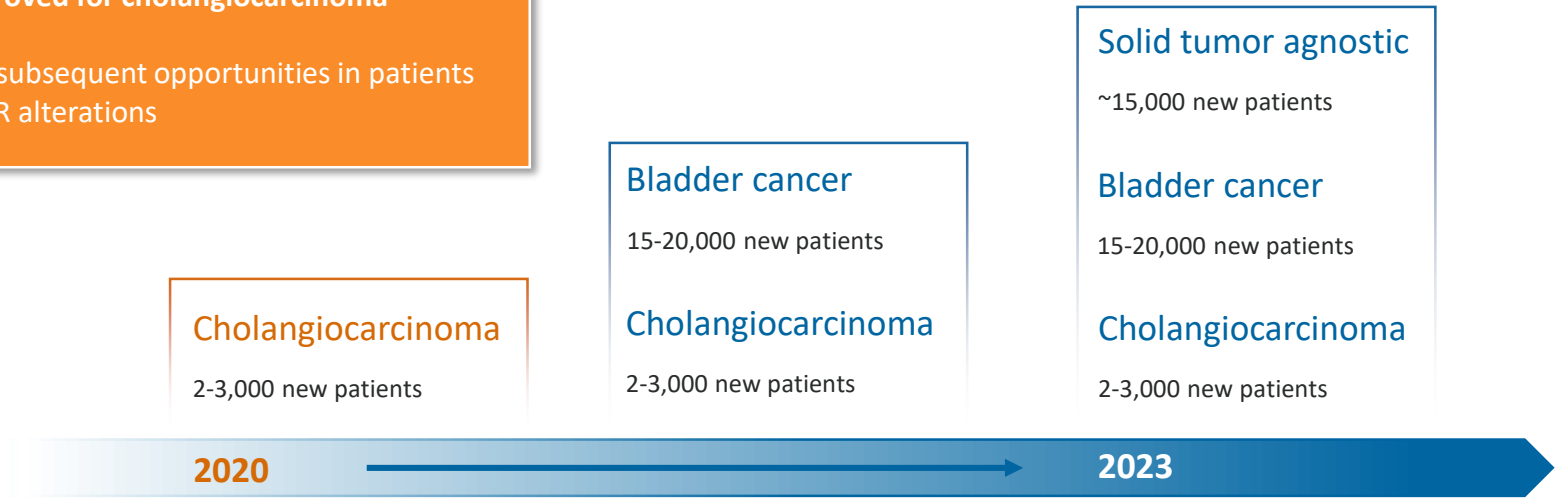

Figure illustrates timelines to first potential in-market approval in each indication.
Patient incidence = estimated number of patients with unresectable / metastatic disease with specific FGFR alteration(s) in US, Europe and Japan.
CCA (intrahepatic): Ann Hepatol. 2018 Mar 1;17(2):274-285; Biochim Biophys Acta Mol Basis Dis. 2018 Apr;1864(4 Pt B):1461-1467; J Natl Compr Canc Netw. 2018 Apr;16(4):370-376; Clin Cancer Res. 2018 Sep 1;24(17):4154-4161; Clin Cancer Res. 2016 Jan 15;22(2):291-300. Bladder: Epidemiology, Decision Resources Group, Bladder: 7/2017; Nature Vol 507 20 March 2014, TCGA; Gust KM, et al. Mol Cancer Ther. 2013;12(7):1245-1254 Tumor agnostic: Endometrial American Cancer Society, NCI; Cancer Research; SEER 2018; EU DRG 2018; IARC, 2017 for France, Italy and Spain; ZfKD, 2016 for Germany and ONS, 2016 for UK; Japan https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5323288/ Japan National Cancer Registry; NIH/American Cancer Society for US death rate; SEER 2018. GBM: Ostrum QT, et al. Neuro Oncol. 2018 Oct 1;20(suppl_4):iv1-iv86; Surveillance of Rare Cancers in Europe (1995-2002), RARECARE [Projected] Other three tumors: Epidemiology, Decision Resources Group: NSCLC: 7/2017; Rectal: 1/2018; H&N: 12/2015.

Q&A

Building Value through Innovative Medicines

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Multiple Opportunities in Patients with Alterations of FGF/FGFR

Opportunities in tumor-defined trials (trials already ongoing)	FGFR alteration		Patient incidence[1]
	Alteration type	Prevalence (%)	
Cholangiocarcinoma	FGFR2 fusions/rearrangements	10-16	2,000-3,000
Bladder cancer	FGFR3 mutations or fusions/rearrangements	15-20	15,000-20,000
8p11 MPN	FGFR1 fusions/rearrangements	100	~100

Example opportunities within tumor-agnostic pivotal trial (expected to start in 2019)	FGFR alteration		Patient incidence[1]
	Alteration type	Prevalence (%)	
Endometrial carcinoma	FGFR2 mutations or fusions/rearrangements	10%	**~15,000** new patients annually with FGF/FGFR alterations
Glioblastoma	FGFR3 mutations or fusions/rearrangements	10%	
Squamous NSCLC	FGFR1, 2 or 3 mutations or fusions/rearrangements	5%	
Rectal cancer	FGFR2 mutations	2%	
SCCHN	FGFR3 mutations or fusions/rearrangements	2%	
Note: There are 12 additional solid tumor types where ≥1% of patients have FGFR1, 2 or 3 mutations or fusions			

1. Patient incidence = estimated number of patients with unresectable / metastatic disease with specific FGFR alteration(s) in US, Europe and Japan.
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